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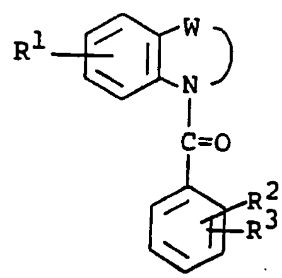
(54) Title: BENZOHETEROCYCLIC COMPOUNDS



(I)

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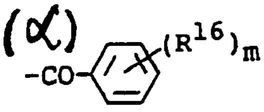

(57) Abstract

Novel benzoheterocyclic compounds of formula (I), wherein R^1 is H, halogen, alkyl, optionally substituted amino, alkoxy; R^2 is H, halogen, alkoxy, phenylalkoxy, OH, alkyl, optionally substituted amino, carbamoyl-alkoxy, optionally substituted amino-alkoxy, optionally substituted benzoyloxy; R^3 is a group: $-NR^4R^5$ or $-CO-NR^{11}R^{12}$; R^4 is H, optionally substituted benzoyl, alkyl; R^5 is a group α [R^{16} is halogen, optionally substituted alkyl, OH, alkoxy, alkanoyloxy, alkylthio, alkanoyl, carboxy, alkoxycarbonyl, CN, NO_2, optionally substituted amino, phenyl, cycloalkyl, etc., or a group: $-O-A-NR^6R^7$; m iş 0 to 3], phenyl-alkoxycarbonyl, alkanoyl, phenyl-alkanoyl, etc.; R^{11} is H or alkyl; R^{12} is cycloalkyl or optionally substituted phenyl; and W is a group: $-(CH_2)_p$ (p is 3 to 5) or $-CH=CH-(CH_2)_q$ (q is 1 to 3), the carbon atom of these groups being optionally replaced by 0, S, SO, SO_2 or a group: $-N(R^{13})-$ and further these groups having optionally 1 to 3 substituents of alkyl, alkoxycarbonyl, carboxy, OH, O, alkanoyloxy, etc., which have excellent vasopressin antagonistic activies and are useful as vasodilator, hypotensive agent, water diuretics, platelet agglutination inhibitor, and a vasopressin antagonistic composition containing the compound as the active ingredient.

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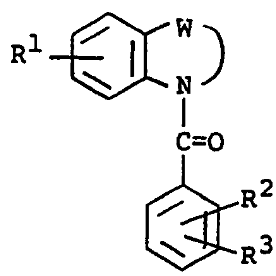
BENZOHETEROCYCLIC COMPOUNDS

Technical Field

This invention relates to novel benzoheterocyclic compounds which have excellent vasopressin antagonistic activities and are useful as vasodilator, hypotensive agent, water diuretics, platelet aggregation inhibitor.

Disclosure of the Invention

The benzoheterocyclic compounds of this invention have the following formula:



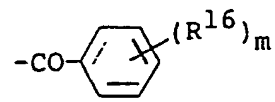
(1)

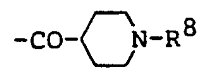
wherein R^1 is hydrogen atom, a halogen atom, a lower alkyl, an amino having optionally a lower alkyl substituent, or a lower alkoxy,

R^2 is hydrogen atom, a halogen atom, a lower alkoxy, a phenyl(lower)alkoxy, hydroxy, a lower alkyl, an amino having optionally a lower alkyl substituent, a carbamoyl-substituted lower alkoxy, an amino-substituted lower alkoxy having optionally a lower alkyl substituent, or a benzoyloxy which has optionally a halogen substituent on the phenyl ring,

R^3 is a group of the formula: $-N\begin{smallmatrix}R^4\\R^5\end{smallmatrix}$ or a group of the formula: $-\overset{O}{\overset{\|}{C}}-N\begin{smallmatrix}R^{11}\\R^{12}\end{smallmatrix}$,

R^4 is hydrogen atom, a benzoyl which has optionally a halogen substituent on the phenyl ring, or a lower alkyl,

R^5 is a group of the formula:  [wherein R^{16} is a halogen atom; a lower alkyl which has optionally a substituent selected from a halogen atom and hydroxy; hydroxy; a lower alkoxy; a lower alkanoyloxy; a lower alkylthio; a lower alkanoyl; carboxy; a lower alkoxycarbonyl; cyano; nitro; an amino which has optionally a substituent selected from a lower alkyl and a lower alkanoyl; phenyl; a cycloalkyl; a lower alkanoyloxy-substituted lower alkoxy; a carboxy-substituted lower alkoxy; a halogen-substituted lower alkoxy; a carbamoyl-substituted lower alkoxy; a hydroxy-substituted lower alkoxy; a lower alkoxycarbonyl-substituted lower alkoxy; a phthalimido-substituted lower alkoxy; an aminocarbonyl-lower alkoxy having a lower alkyl substituent; or a group of the formula: $-O-A-N\begin{matrix} \diagup R^6 \\ \diagdown R^7 \end{matrix}$ (A is a lower alkylene, and R^6 and R^7 are the same or different and are each hydrogen atom, a lower alkyl having optionally a hydroxy substituent, a lower alkanoyl, or benzoyl, or R^6 and R^7 may bind together with nitrogen atom to which they bond to form a 5- or 6-membered saturated heterocyclic group with or without being intervened with nitrogen or oxygen atom wherein the heterocyclic group has optionally a substituent selected from piperidinyl and a lower alkyl); and m is an integer of 0 to 3], a phenyl-lower alkoxycarbonyl, a lower alkanoyl, a phenyl-

lower alkanoyl, a cycloalkyl-lower alkanoyl, a cycloalkylcarbonyl, tricyclo[3.3.1.1]decanylcarbonyl, naphthylcarbonyl, pyridylcarbonyl, furoyl, thenoyl, a phenoxy-lower alkanoyl which phenyl ring has optionally 1 to 3 substituents selected from a lower alkyl, a lower alkoxy and an amino having optionally a lower alkanoyl substituent, a phthalimido-substituted lower alkanoyl, a lower alkoxycarbonyl-lower alkanoyl, a carboxy-lower alkanoyl, a naphthyloxy-lower alkanoyl, a halogen-substituted lower alkanoyl, a group of the formula:  (wherein R^8 is hydrogen atom, a lower alkyl, a phenyl-lower alkoxycarbonyl, a carbamoyl-lower alkyl, an amino-lower alkanoyl having optionally a lower alkyl substituent, or a lower alkanoyl), an anilinocarbonyl which has optionally a lower alkyl substituent on the phenyl ring, phenoxycarbonyl, a phenylsulfonyl which has optionally a substituent selected from a halogen atom and a lower alkyl on the phenyl ring, quinolylsulfonyl, or a group of the formula:

$-CO-B-(CO)_n-N{<}^{R^9}_{R^{10}}$ (wherein B is a lower alkylene, n is an integer of 0 or 1, and R^9 and R^{10} are the same or different and are each hydrogen atom, a lower alkyl having optionally a hydroxy substituent, a cycloalkyl, a phenyl-lower alkyl, a lower alkanoyl, a lower alkenyl, a phenoxy-lower alkyl, a phenyl which has optionally 1 to 3 substituents selected from an amino-lower alkyl having optionally a lower alkanoyl substituent, a lower alkyl, a lower alkoxy and a halogen atom, a phthalimido-substituted lower alkyl, an amino-lower

alkyl having optionally a lower alkanoyl substituent, a lower alkynyl, or an amino-lower alkyl having optionally a lower alkyl substituent, or R^9 and R^{10} may bind together with nitrogen atom to which they bond to form a 5- or 6-membered saturated heterocyclic group with or without being intervened with nitrogen or oxygen atom wherein the hetero-cylic group has optionally a substituent selected from a lower alkyl, a lower alkoxycarboyl and piperidinyl),

R^{11} is hydrogen atom or a lower alkyl,

R^{12} is a cycloalkyl, or a phenyl which has optionally 1 to 3 substituents selected from a lower alkoxy, a lower alkyl and a halogen atom,

W is a group of the formula: $-(CH_2)_p-$ (p is an integer of 3 to 5), or a group of the formula: $-CH=CH-(CH_2)_q-$ (q is an integer of 1 to 3), the carbon atom of these groups: $-(CH_2)_p-$ and $-CH=CH-(CH_2)_q-$ being optionally replaced by oxygen atom, sulfur atom, sulfinyl, sulfonyl, or a group of the formula: $\overset{\displaystyle R^{13}}{\overset{|}{-N-}}$ (R^{13} is hydrogen atom, a cycloalkyl, or a lower alkyl), and further said $-(CH_2)_p-$ and $-CH=CH-(CH_2)_q-$ groups having optionally 1 to 3 substituents selected from a lower alkyl having optionally a hydroxy substituent, a lower alkoxycarbonyl, carboxy, hydroxy, oxo, a lower alkanoyloxy having optionally a halogen substituent, an amino-lower alkyl naving optionally a substituent selected from a lower alkyl and a lower alkanoyl, a lower alkanoyloxy-substituted lower alkyl, a lower alkyl sulfonyloxy-lower alkyl, an

azido-lower alkyl, a group of the formula: , an aminocarbonyloxy having optionally a lower alkyl substituent, a lower alkoxy, a lower alkoxycarbonyl-substituted lower alkoxy, a carboxy-substituted lower alkoxy, an aminocarbonyl-lower alkoxy having optionally a lower alkyl substituent, an amino-lower alkoxy having optionally a substituent selected from a lower alkyl and a lower alkanoyl, a phthalimido-substituted lower alkoxy, hydroxyimino, a lower alkanoyloxy-imino, a lower alkylidene, a halogen atom, azido, sulfoxyimino, a group of the formula: $R^{81}\text{-}\underset{|}{N}\text{-}CH_2COO\text{-}$ (R^{81} is hydrogen atom or a lower alkyl), hydrazino, pyrrolyl, an amino-lower alkanoyloxy having optionally a lower alkyl substituent, a group of the formula: $-O-A-CO-N{\lessgtr}^{R^{82}}_{R^{83}}$ (A is as defined above, and R^{82} and R^{83} are the same or different and are each hydrogen atom, a lower alkyl, a carbamoyl-substituted lower alkyl, a hydroxy-substituted lower alkyl, or a pyridyl-lower alkyl, or R^{82} and R^{83} may bind together with nitrogen atom to which they bond to form a 5- or 6-membered saturated heterocyclic group with or without being intervened with nitrogen, oxygen or sulfur atom wherein the heterocyclic group has optionally a substituent selected from oxo, a lower alkyl, a lower alkanoyl, and carbamoyl), and a group of the formula: $-(CO)_n-N{\lessgtr}^{R^{14}}_{R^{15}}$ (wherein n is as defined above, and R^{14} and R^{15}

are the same or different and are each hydrogen atom, a lower alkyl, a lower alkenyl, a lower alkanoyl, a cycloalkyl, an oxiranyl-substituted lower alkyl, a lower alkyl having optionally 1 to 2 substituents selected from a lower alkoxy, hydroxy and an amino having optionally a lower alkyl substituent, a phenyl-lower alkyl, a pyridyl-lower alkyl, a lower alkylsulfonyl, benzoyl, a lower alkoxy-carbonyl, anilinocarbonyl, an aminocarbonyl having optionally a lower alkyl substituent, a cyano-substituted lower alkyl, a lower alkoxycarbonyl-substituted lower alkyl, a carbamoyl-substituted lower alkyl, a carboxy-substituted lower alkyl, a tetrahydropyranyloxy-substituted lower alkyl, a lower alkanoyloxy-substituted lower alkyl, a piperidinyl having optionally a phenyl-lower alkyl substituent on the piperidinyl ring, a halogen-substituted lower alkanoyl, an imidazolyl-substituted lower alkanoyl, an amino-lower alkanoyl having optionally a substituent selected from a lower alkyl and a lower alkoxycarbonyl, an aminocarbonyl-lower alkyl having optionally a lower alkyl substituent, or a phenyl-lower alkoxycarbonyl, or R^{14} and R^{15} may bind together with nitrogen atom to which they bond to form a 5- or 6-membered saturated heterocyclic group with or without being intervened with nitrogen or oxygen, wherein the heterocyclic group may optionally have a substituent selected from a lower alkyl, a phenyl-lower alkyl or a lower alkanoyl).

The benzoheterocyclic compounds of the formula (1) and

their salts have excellent vasopressin antagonistic activities and vasodilating activity, hypotensive activity, activity for inhibiting saccharide release in liver, activity for inhibiting growth of mesangium cells, water diuretic activity, platelet agglutination inhibitory activity and are useful as vasodilator, hypotensive agent, water diuretics, platelet agglutination inhibitor and are used for the prophylaxis and treatment of hypertension, edema, ascites, heart failure, renal function disorder, vasopressin parasecretion syndrome (SIADH), hepatocirrhosis, hyponatremia, hypokaliemia, diabetic, circulation disorder, and the like.

Each group in the above formula (1) includes specifically the following groups.

The "lower alkoxy" includes a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms, for example, methoxy, ethoxy, propoxy, isopropoxy, butoxy, tert-butoxy, pentyloxy, hexyloxy, and the like.

The "lower alkyl" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, pentyl, hexyl, and the like.

The "halogen atom" includes fluorine atom, chlorine atom, bromine atom and iodine atome.

The "amino having optionally a lower alkyl substituent" includes an amino having optionally one or two substituents selected from a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, amino,

methylamino, ethylamino, propylamino, isopropylamino, butylamino, tert-butylamino, pentylamino, hexylamino, dimethylamino, diethylamino, dipropylamino, dibutylamino, dipentylamino, dihexylamino, N-methyl-N-ethylamino, N-ethyl-N-propylamino, N-methyl-N-butylamino, N-methyl-N-hexylamino, and the like.

The "lower alkenyl" includes a straight chain or branched chain alkenyl group having 2 to 6 carbon atoms, for example, vinyl, allyl, 2-butenyl, 3-butenyl, 1-methylallyl, 2-pentenyl, 2-hexenyl, and the like.

The "lower alkyl which has optionally a substituent selected from a halogen atom and hydroxy" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which may optionally have 1 to 3 substituents selected from a halogen atom and hydroxy, for example, in addition to the above-mentioned lower alkyl groups, hydroxymethyl, 2-hydroxyethyl, 1-hydroxyethyl, 3-hydroxypropyl, 2,3-dihyroxypropyl, 4-hydroxybutyl, 1,1-dimethyl-2-hydroxyethyl, 5,5,4-trihydroxypentyl, 5-hydroxypentyl, 6-hydroxyhexyl, 1-hydroxyisopropyl, 2-methyl-3-hydroxypropyl, trifluoromethyl, trichloromethyl, chloromethyl, bromomethyl, fluoromethyl, iodomethyl, difluoromethyl, dibromomethyl, 2-chloroethyl, 2,2,2-trifluoroethyl, 2,2,2-trichloroethyl, 3-chloropropyl, 2,3-dichloropropyl, 4,4,4-trichlorobutyl, 4-fluorobutyl, 5-chloropentyl, 3-chloro-2-methylpropyl, 5-bromohexyl, 5,6-dichlorohexyl, and the like.

The "lower alkylene" includes a straight chain or

branched chain alkylene group having 1 to 6 carbon atoms, for example, methylene, ethylene, trimethylene, 2-methyltrimethylene, 2,2-dimethyltrimethylene, 1-methyltrimethylene, methylmethylene, ethylmethylene, tetramethylene, pentamethylene, hexamethylene, and the like.

The "lower alkanoyloxy" includes a straight chain or branched chain alkanoyloxy group having 1 to 6 carbon atoms, for example, formyloxy, acetyloxy, propionyloxy, butyryloxy, isobutyryloxy, pentanoyloxy, tert-butylcarbonyloxy, hexanoyloxy, and the like.

The "lower alkylthio" includes a straight chain or branched chain alkylthio group having 1 to 6 carbon atoms, for example, methylthio, ethylthio, propylthio, isopropylthio, butylthio, tert-butylthio, pentylthio, hexylthio, and the like.

The "lower alkanoyl" includes a straight chain or branched chain alkanoyl group having 1 to 6 carbon atoms, for example, formyl, acetyl, propionyl, butyryl, isobutyryl, pentanoyl, tert-butylcarbonyl, hexanolyl, and the like.

The "lower alkoxycarbonyl" includes a straight chain or branched chain alkoxycarbonyl group having 1 to 6 carbon atoms in the alkoxy moiety, for example, methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, tert-butoxycarbonyl, pentyloxycarbonyl, hexyloxycarbonyl, and the like.

The "amino having optionally a substituent selected from a lower alkyl and a lower alkanoyl" includes an amino having optionally one or two substituents selected from a

straight chain or branched chain alkyl group having 1 to 6 carbon atoms and a straight chain or branched chain alkanoyl group having 1 to 6 carbon atoms, for example, amino, methylamino, ethylamino, propylamino, isopropylamino, butylamino, tert-butylamino, pentylamino, hexylamino, dimethylamino, diethylamino, dipropylamino, dibutylamino, dipentylamino, dihexylamino, N-methyl-N-ethylamino, N-ethyl-N-propylamino, N-methyl-N-butylamino, N-methyl-N-hexylamino, N-methyl-N-acetylamino, N-acetylamino, N-formylamino, N-propionylamino, N-butyrylamino, N-isobutyrylamino, N-pentanoylamino, N-tert-butylcarbonylamino, N-hexanoylamino, N-ethyl-N-acetylamino, and the like.

The "cycloalkyl" includes a cycloalkyl having 3 to 8 carbon atoms, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, and the like.

The "lower alkanoyloxy-substituted lower alkoxy" includes a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms which is substituted by a straight chain or branched chain alkanoyloxy group having 2 to 6 carbon atoms, for example, acetyloxymethoxy, 2-propionyloxyethoxy, 1-butyryloxyethoxy, 3-acetyloxypropoxy, 4-acetyloxybutoxy, 4-isobutyryloxybutoxy, 5-pentanoyloxypentyloxy, 6-acetyloxyhexyloxy, 6-tert-butylcarbonyloxyhexyloxy, 1,1-dimethyl-2-hexanoyloxyethoxy, 2-methyl-3-acetyloxypropoxy, and the like.

The "carbamoyl-substituted lower alkoxy" includes a carbamoyl-substituted alkoxy group wherein the alkoxy moiety is a straight chain or branched chain alkoxy group having 1 to 6

carbon atoms, for example, carbamoylmethoxy, 2-carbamoylethoxy, 1-carbamoylethoxy, 3-carbamoylpropoxy, 4-carbamoylbutoxy, 5-carbamoylpentyloxy, 6-carbamoylhexyloxy, 1,1-dimethyl-2-carbamoylethoxy, 2-methyl-3-carbamoylpropoxy, and the like.

The "hydroxy-substituted lower alkoxy" includes a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms and having 1 to 3 hydroxy substitutents, for example, hydroxymethoxy, 2-hydroxyethoxy, 1-hydroxyethoxy, 3-hydroxypropoxy, 2,3-dihydroxypropoxy, 4-hydroxybutoxy, 3,4-dihydroxybutoxy, 1,1-dimethyl-2-hydroxyethoxy, 5-hydroxy-pentyloxy, 6-hydroxyhexyloxy, 2-metnyl-3-hydroxypropoxy, 2,3,4-trihydroxybutoxy, and the like.

The "lower alkoxycarbonyl-substituted lower alkoxy" includes an alkoxycarbonyl-substituted straight chain or branched chain alkoxy group having 1 to 6 carbon atoms wherein the alkoxycarbonyl moiety is a straight chain or branched chain alkoxycarbonyl group having 1 to 6 carbon atoms, for example, methoxycarbonylmethoxy, 3-methoxycarbonylpropoxy, ethoxy-carboxymethoxy, 3-ethoxycarbonylpropoxy, 4-ethoxycarbonyl-butoxy, 5-isopropoxycarbonylpentyloxy, 6-propoxycarbonyl-hexyloxy, 1,1-dimethyl-2-butoxycarbonylethoxy, 2-methyl-3-tert-butoxycarbonylpropoxy, 2-pentyloxycarbonylethoxy, hexyloxy-carbonylmethoxy, and the like.

The "carboxy-substituted lower alkoxy" includes a carboxy-substituted alkoxy group wherein the alkoxy moiety is a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms, for example, carboxymethoxy, 2-carboxyethoxy, 1-

carboxyethoxy, 3-carboxypropoxy, 4-carboxybutoxy, 5-carboxypentyloxy, 6-carboxyhexyloxy, 1,1-dimethyl-2-carboxyethoxy, 2-methyl-3-carboxypropoxy, and the like.

The "phthalimido-substituted lower alkoxy" includes a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms which is substituted by phthalimido group, for example, phthalimidomethoxy, 2-phthalimidoethoxy, 1-phthalimidoethoxy, 3-phthalimidopropoxy, 4-phthalimidobutoxy, 5-phthalimidopentyloxy, 6-phthalimidohexyloxy, 1,1-dimethyl-2-phthalimidoethoxy, 2-methyl-3-phthalimidopropoxy, and the like.

The "5- or 6-membered saturated heterocyclic group which is formed by binding the groups R^6 and R^7 together with the nitrogen atom to which they bond with or without being intervened with nitrogen or oxygen atom" includes, for example, pyrrolidinyl, piperidinyl, piperazinyl, morpholino, and the like.

The "heterocyclic group having a substituent selected from piperidinyl and a lower alkyl" includes a heterocyclic group having 1 to 3 substituents selected from piperidinyl and a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, 4-methylpiperiazinyl, 3,4-dimethylpiperazinyl, 3-ethylpyrrolidinyl, 2-propylpyrrolidinyl, 3,4,5-trimethylpiperidinyl, 4-butylpiperidinyl, 3-pentylmorpholino, 4-hexylpiperazinyl, 4-(1-piperidinyl)piperidinyl, 3-(1-piperidinyl)pyrrolidinyl, 3-(1-piperidinyl)-4-methylpiperazinyl, 3-(1-piperidinyl)morpholino, and the like.

The "phenyl(lower)alkanoyl" includes a phenylalkanoyl wherein the alkanoyl moiety is a straight chain or branched

chain alkanoyl group having 2 to 6 carbon atoms, for example, phenylacetyl, 3-phenylpropionyl, 2-phenylpropionyl, 4-phenylbutyryl, 2,2-dimethyl-3-phenylpropionyl, 5-phenylpentanoyl, 6-phenylhexanoyl, and the like.

The "cycloalkyl-lower alkanoyl" includes C_3-C_8 cycloalkyl-alkanoyl group wherein the alkanoyl moiety is a straight chain or branched chain alkanoyl having 2 to 6 carbon atoms, for example, cyclohexylacetyl, 3-cyclopropylpropionyl, 2-cyclopentylpropionyl, 4-cyclohexylbutyryl, 2,2-dimethyl-3-cycloheptylpropionyl, 5-cyclooctylpentanoyl, 6-cyclohexylhexanoyl, and the like.

The "cycloalkylcarbonyl" includes a cycloalkylcarbonyl having 3 to 8 carbon atoms, for example, cyclopropylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, cycloheptylcarbonyl, cyclooctylcarbonyl, and the like.

The "amino having optionally a lower alkanoyl substituent" includes an amino having optionally a straight chain or branched chain alkanoyl group having 1 to 6 carbon atoms, for example, amino, formylamino, acetylamino, propionylamino, butyrylamino, isobutyrylamino, pentanoylamino, tert-butylcarbonylamino, hexanoylamino, and the like.

The "phenoxy-lower alkanoyl which phenyl ring has optionally 1 to 3 substituents selected from a lower alkyl, a lower alkoxy and an amino having optonally a lower alkanoyl substituent" includes a phenoxyalkanoyl group wherein the alkanoyl moiety is a straight chain or branched chain alkanoyl having 2 to 6 carbon atoms and the phenyl ring has optionally 1

to 3 substituents selected from a straight chain or branched chain alkyl having 1 to 6 carbon atoms, a straight chain or branched chain alkoxy having 1 to 6 carbon atoms and an amino having optionally a straight chain or branched chain alkanoyl having 1 to 6 carbon atoms, for example, phenoxyacetyl, 3-phenoxypropionyl, 2-phenoxypropionyl, 4-phenoxybutyryl, 2,2-dimethyl-3-phenoxypropionyl, 5-phenoxypentanoyl, 6-phenoxyhexanoyl, (2-aminophenoxy)acetyl, 3-(4-aminophenoxy)propionyl, (2-methylphenoxy)acetyl, (4-methylphenoxy)acetyl, (3-methylphenoxy)acetyl, (3-methoxyphenoxy)acetyl, (3-acetylaminophenoxy)acetyl, 4-(2-propionylaminophenoxy)butyryl, 2,2-dimethyl-3-(4-butyrylaminophenoxy)propionyl, 5-(2-pentanoylaminophenoxy)pentanoyl, 6-(4-hexanoylaminophenoxy)hexanoyl, 3-(2-ethylphenoxy)propionyl, 2-(4-propylphenoxy)propionyl, 4-(4-butylphenoxy)butyryl, 5-(3-pentylphenoxy)pentanoyl, 6-(4-hexylphenoxy)hexanoyl, (2,3-dimethylphenoxy)acetyl, (2,5-dimethylphenoxy)acetyl, (3,4-dimethylphenoxy)acetyl, (3,4,5-trimethylphenoxy)acetyl, 3-(4-ethoxyphenoxy)propionyl, 2-(2-propoxyphenoxy)propionyl, 4-(3-butoxyphenoxy)butyryl, 5-(4-pentyloxyphenoxy)pentanoyl, 6-(4-hexyloxyphenoxy)hexanoyl, (3,4-dimethoxyphenoxy)acetyl, (3,5-dimethoxyphenoxy)acetyl, (2,4-dimethoxyphenoxy)acetyl, (3,4,5-trimethoxyphenoxy)acetyl, (2-acetylamino-4-methylphenoxy)acetyl, (4-acetylamino-3-methoxyphenoxy)acetyl, and the like.

The "phthalimido-substituted lower alkanoyl" includes a straight chain or branched chain alkanoyl group having 2 to 6 carbon atoms which is substituted by phthalimido group, for

example, 2-phthalimidoacetyl, 3-phthalimidopropionyl, 2-phthalimidopropionyl, 4-phthalimidobutyryl, 2,2-dimethyl-3-phthalimidopropionyl, 5-phthalimidopentanoyl, 6-phthalimidohexanoyl, 3-methyl-4-phthalimidobutyryl, and the like.

The "lower alkoxycarbonyl-lower alkanoyl" includes an alkoxycarbonyl-alkanoyl group wherein the alkoxy moiety is a straight chain or branched chain alkoxy having 1 to 6 carbon atoms and the alkanoyl moiety is a straight chain or branched chain alkanoyl having 2 to 6 carbon atoms, for example, methoxycarbonylacetyl, 3-methoxycarbonylpropionyl, ethoxycarbonylacetyl, 3-ethoxycarbonylpropionyl, 4-ethoxycarbonylbutyryl, 3-propoxycarbonylpropionyl, 2-methoxycarbonylpropionyl, 6-propoxycarbonylhexanoyl, 5-isopropoxycarbonylpentanoyl, 2,2-dimethyl-3-butoxycarbonylpropionyl, 2-methyl-3-tert-butoxycarbonylpropionyl, pentyloxycarbonylacetyl, hexyloxycarbonylacetyl, and the like.

The "carboxy-lower alkanoyl" includes a carboxyalkanoyl group wherein the alkanoyl moiety is a straight chain or branched chain alkanoyl having 2 to 6 carbon atoms, for example, carboxyacetyl, 3-carboxypropionyl, 2-carboxypropionyl, 4-carboxybutyryl, 2,2-dimethyl-3-carboxypropionyl, 5-carboxypentanoyl, 6-carboxyhexanoyl, and the like.

The "naphthyloxy-lower alkanoyl" includes a naphthyloxy-alkanoyl group wherein the alkanoyl moiety is a straight chain or branched chain alkanoyl having 2 to 6 carbon atoms, for example, naphtyloxyacetyl, 3-naphtyloxypropionyl, 2-naphtyloxypropionyl, 4-naphthyloxybutyryl, 2,2-dimethyl-3-

naphthyloxypropionyl, 5-naphthyloxypentanoyl, 6-naphthyloxyhexanoyl, and the like.

The "phenyl-lower alkoxycarbonyl" includes a phenylalkoxycarbonyl wherein the alkoxycarbonyl moiety is a straight chain or branched chain alkoxycarbonyl group having 1 to 6 carbon atoms, for example, benzyloxycarbonyl, 2-phenylethoxycarbonyl, 1-phenylethoxycarbonyl, 3-phenylpropoxycarbonyl, 4-phenylbutoxycarbonyl, 5-phenylpentyloxycarbonyl, 6-phenylhexyloxycarbonyl, 1,1-dimethyl-2-phenylethoxycarbonyl, 2-methyl-3-phenylpropoxycarbonyl, and the like.

The "lower alkyl having optionally a hydroxy substituent" includes a straight chain or branched chain alkyl having 1 to 6 carbon atoms and having optionally 1 to 3 hydroxy substituents, for example, hydroxymethyl, 2-hydroxyethyl, 1-hydroxyethyl, 3-hydroxypropyl, 2,3-dihydroxyethyl, 4-hydroxybutyl, 3,4-dihydroxybutyl, 1,1-dimethyl-2-hydroxyethyl, 5-hydroxypentyl, 6-hydroxyhexyl, 2-methyl-3-hydroxypropyl, 2,3,4-trihydroxybutyl, and the like.

The "phenyl-lower alkyl" includes a phenylalkyl group wherein the alkyl moiety is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, benzyl, 2-phenylethyl, 1-phenylethyl, 3-phenylpropyl, 4-phenylbutyl, 5-phenylpentyl, 6-phenylhexyl, 1,1-dimethyl-2-phenylethyl, 2-methyl-3-phenylpropyl, and the like.

The "phenoxy-lower alkyl" includes a phenoxyalkyl group wherein the alkyl moiety is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example,

phenoxymethyl, 1-phenoxyethyl, 2-phenoxyethyl, 3-phenoxypropyl, 4-phenoxybutyl, 5-phenoxypentyl, 6-phenoxyhexyl, 1,1-dimethyl-2-phenoxyethyl, 2-methyl-3-phenoxypropyl, and the like.

The "phenyl which has optionally 1 to 3 substituents selected from a lower alkyl, a lower alkoxy and a halogen atom" includes a phenyl group which has optionally 1 to 3 substituents selected from a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms and a halogen atom, for example, phenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-ethoxyphenyl, 3-ethoxyphenyl, 4-ethoxyphenyl, 4-isopropoxyphenyl, 4-pentyloxyphenyl, 2,4-dimethoxyphenyl, 4-hexyloxyphenyl, 3,4-dimethoxyphenyl, 3-ethoxy-4-methoxyphenyl, 2,3-dimethoxyphenyl, 3,4-diethoxyphenyl, 2,5-dimethoxyphenyl, 2,6-dimethoxyphenyl, 3,5-dimethoxyphenyl, 3,4-dipentyloxyphenyl, 3,4,5-trimethoxyphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-bromophenyl, 3-bromophenyl, 4-bromophenyl, 2-iodophenyl, 3-iodophenyl, 4-iodophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 2,6-dichlorophenyl, 2,3-dichlorophenyl, 2,4-dichlorophenyl, 3,4-difluorophenyl, 3,5-dibromophenyl, 3,4,5-trichlorophenyl, 2-methoxy-3-chlorophenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-ethylphenyl, 3-ethylphenyl, 4-ethylphenyl, 4-isopropylphenyl, 3-butylphenyl, 4-pentylphenyl, 4-hexylphenyl, 3,4-dimethylphenyl, 3,4-diethylphenyl, 2,4-dimethylphenyl, 2,5-dimethylphenyl, 2,6-dimethylphenyl, 3,4,5-trimethylphenyl, 3-chloro-4-methylphenyl, 3-methoxy-4-methyl-5-

iodophenyl, 3,4-dimethoxy-5-bromophenyl, 3,5-diiodo-4-methoxyphenyl, and the like.

The "amino-lower alkyl having optionally a lower alkyl substituent" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by an amino group having optionally 1 to 2 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, aminomethyl, 2-aminoethyl, 1-aminoethyl, 3-aminopropyl, 4-aminobutyl, 5-aminopentyl, 6-aminohexyl, 1,1-dimethyl-2-aminoethyl, 2-methyl-3-aminopropyl, methylaminomethyl, 1-ethylaminoethyl, 2-propylaminoethyl, 3-isopropylaminopropyl, 4-butylaminobutyl, 5-pentylaminopentyl, 6-hexylaminohexyl, dimethylaminomethyl, (N-ethyl-N-propylamino)methyl, 2-(N-methyl-N-hexylamino)ethyl, and the like.

The "5- or 6-membered saturated heterocyclic group which is formed by binding the groups R^9 and R^{10} together with the nitrogen atom to which they bond with or without being intervened with nitrogen or oxygen atom" includes, for example, pyrrolidinyl, piperidinyl, piperazinyl, morpholino, and the like.

The "heterocyclic group having a substituent selected from a lower alkyl, a lower alkoxycarbonyl and piperidinyl" includes a heterocyclic group having 1 to 3 substituents selected from a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, a straight chain or branched chain alkoxycarbonyl having 1 to 6 carbon atoms and piperidinyl, for example, in addition to the above-mentioned heterocyclic groups

having a substituent of a lower alkyl and piperidinyl, 4-methoxycarbonylpiperazinyl, 4-ethoxycarbonylpiperidinyl, 3-propoxycarbonylpyrrolidinyl, 2-pentyloxycarbonylmorpholino, 4-hexyloxycarbonylpiperidinyl, 4-ethoxycarbonyl-3-methyl-piperidinyl, 3-methyl-4-ethoxycarbonylpiperazinyl, and the like.

The "5- or 6-membered saturated heterocyclic group which is formed by binding the groups R^{14} and R^{15} together with the nitrogen atom to which they bond with or without being intervened with nitrogen or oxygen atom" includes, for example, pyrrolidinyl, piperidinyl, piperazinyl, morpholino, and the like.

The "heterocyclic group having a lower alkyl substituent" includes a heterocyclic group having 1 to 3 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, 4-methylpiperazinyl, 3,4-dimethylpiperazinyl, 3-ethylpyrrolidinyl, 2-propyl-pyrrolidinyl, 3,4,5-trimethylpiperidinyl, 4-butylpiperidinyl, 3-pentylmorpholino, 4-hexylpiperazinyl, and the like.

The heterocyclic ring in the formula (1) includes tetrahydroquinolyl, 2,3,4,5-tetrahydro-1H-benzazepinyl, 1,2,3,4,5,6-hexahydrobenzazocinyl, 1,2-dihydroquinolyl, 2,3-dihydro-1H-benzazepinyl, 1,2,3,4-tetrahydrobenzazocinyl, and the like.

The heterocyclic ring in the formula (1) wherein the carbon atom in the group of the formula: $-(CH_2)_p-$ or $-CH=CH-(CH_2)_q-$ for W is replaced by oxygen atom, sulfur atom,

sulfinyl, sulfonyl, or a group of the formula: $-\overset{R^{13}}{\overset{|}{N}}-$ (R^{13} is hydrogen atom or a lower alkyl) includes a heterocylic group wherein the carbon atom in the group of the formula: $-(CH_2)_p-$ or $-CH=CH-(CH_2)_q-$ for W is replaced by oxygen atom, sulfur atom, sulfinyl, sulfonyl, or a group of the formula: $-\overset{R^{13}}{\overset{|}{N}}-$ (R^{13} is hydrogen atom or a straight chain or branched chain alkyl having 1 to 6 carbon atoms), for example, 3,4-dihydro-2H-1,4-benzoxazinyl, 1,2,3,5-tetrahydro-4,1-benzoxazepinyl, 1,2,3,4-tetrahydroquinoxalinyl, 1,2,3,4,5,6-hexahydro-1,5-benzodiazocinyl, 5-methyl-1,2,3,4,5,6-hexahydro-1,5-benzodiazocinyl, 4-methyl-1,2,3,4-tetrahydroquinoxalinyl, 1,2,3,4-tetrahydro-5,1-benzoxazepinyl, 3,4-dihydro-2H-1,4-benzothiazinyl, 2,3,4,5-tetrahydro-1,5-benzothiazepinyl, 1,2,3,5-tetrahydro-4,1-benzothiazepinyl, 4-ethyl-1,2,3,4-tetrahydroquinoxalinyl, 4-propyl-1,2,3,4-tetrahydroquinoxalinyl, 4-butyl-1,2,3,4-tetrahydroquinoxalinyl, 4-pentyl-1,2,3,4-tetrahydroquinoxalinyl, 4-hexyl-1,2,3,4-tetrahydroquinoxalinyl, 2,3,4,5-tetrahydro-1H-1,4-benzodiazepinyl, 4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepinyl, 4-ethyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepinyl, 4-propyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepinyl, 4-butyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepinyl, 4-pentyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepinyl, 4-hexyl-2,3;4,5-tetrahydro-1H-1,4-benzodiazepinyl, 2,3,4,5-tetrahydro-1H-1,5-benzodiazepinyl, 5-methyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepinyl, 5-ethyl-2,3,4,5-tetrahydro-1H-1,5-benzo-

diazepinyl, 5-propyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepinyl, 5-butyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepinyl, 5-pentyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepinyl, 5-hexyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepinyl, 3,4-dihydro-1-oxo-2H-1,4-benzothiazepinyl, 3,4-dihydro-1,1-dioxo-2H-1,4-benzothiazepinyl, 1-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepinyl, 1,1-dioxo-2,3,4,5-tetrahydro-1,5-benzothiazepinyl, 4-oxo-1,2,3,5-tetrahydro-4,1-benzothiazepinyl, 4,4-dioxo-1,2,3,5-tetrahydro-4,1-benzothiazepinyl, and the like.

The "halogen-substituted lower alkoxy" includes a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms which has 1 to 3 substituents of a halogen atom, for example, trifluoromethoxy, trichloromethoxy, chloromethoxy, bromomethoxy, fluoromethoxy, iodomethoxy, difluoromethoxy, dibromomethoxy, 2-chloroethoxy, 2,2,2-trifluoroethoxy, 2,2,2-trichloroethoxy, 3-chloropropoxy, 2,3-dichloropropoxy, 4,4,4-trichlorobutoxy, 4-fluorobutoxy, 5-chloropentyloxy, 3-chloro-2-methylpropoxy, 6-bromohexyloxy, 5,6-dichlorohexyloxy, and the like.

The "halogen-substituted lower alkanoyl" includes a straight chain or branched chain alkanoyl group having 1 to 6 carbon atoms which has 1 to 3 substituents of a halogen atom, for example, 2,2,2-trifluoroacetyl, 2,2,2-trichloroacetyl, 2-chloroacetyl, 2-bromoacetyl, 2-fluoroacetyl, 2-iodoacetyl, 2,2-difluoroacetyl, 2,2-dibromoacetyl, 3,3,3-trifluoropropionyl, 3,3,3-trichloropropionyl, 3-chloropropionyl, 2,3-dichloropropionyl, 4,4,4-trichlorobutyryl, 4-fluorobutyryl, 5-

chloropentanoyl, 3-chloro-2-methylpropionyl, 6-bromohexanoyl, 5,6-dibromohexanoyl, and the like.

The "aminocarbonyl-lower alkoxy having a lower alkyl substituent" includes a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms which is substituted by an aminocarbonyl group having 1 to 2 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, methylaminocarbonylmethoxy, 1-ethylaminocarbonylethoxy, 2-propylaminocarbonylethoxy, 3-isopropylaminocarbonylpropoxy, 4-butylaminocarbonylbutoxy, 5-pentylaminocarbonylpentyloxy, 6-hexylaminocarbonylhexyloxy, dimethylaminocarbonylmethoxy, 3-diethylaminocarbonylpropoxy, diethylaminocarbonylmethoxy, (N-ethyl-N-propylamino)carbonylmethoxy, 2-(N-methyl-N-hexylamino)carbonylethoxy, and the like.

The "carbamoyl-lower alkyl" includes a carbamoyl-substituted alkyl group wherein the alkyl moiety is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, carbamoylmethyl, 2-carbamoylethyl, 1-carbamoylethyl, 3-carbamoylpropyl, 4-carbamoylbutyl, 5-carbamoylpentyl, 6-carbamoylhexyl, 1,1-dimethyl-2-carbamoylethyl, 2-methyl-3-carbamoylpropyl, and the like.

The "amino-lower alkanoyl having optionally a lower alkyl substituent" includes a straight chain or branched chain alkanoyl having 2 to 6 carbon atoms which is substituted by an amino group having optionally 1 to 2 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, 2-aminoacetyl, 3-aminopropionyl, 2-aminopropionyl,

4-aminobutyryl, 5-aminopentanoyl, 6-aminohexanoyl, 2,2-dimethyl-3-aminopropionyl, 2-methyl-3-aminopropionyl, 2-methylaminoacetyl, 2-ethylaminopropionyl, 3-propylaminopropionyl, 3-isopropylaminopropionyl, 4-butylaminobutyryl, 5-pentylaminopentanoyl, 6-hexylaminohexanoyl, 2-dimethylaminoacetyl, 2-diethylaminoacetyl, 2-(N-ethyl-N-propylamino)acetyl, 3-(N-methyl-N-hexylamino)propionyl, and the like.

The "amino-lower alkyl having optionally a lower alkanoyl substituent" includes a straight chain or branched chain alkyl having 1 to 6 carbon atoms which is substituted by an amino group having optionally a substituent of a straight chain or branched chain alkanoyl group having 1 to 6 carbon atoms, for example, aminomethyl, 2-aminoethyl, 1-aminoethyl, 3-aminopropyl, 4-aminobutyl, 5-aminopentyl, 6-aminohexyl, 1,1-dimethyl-2-aminoethyl, 2-methyl-3-aminopropyl, acetylaminomethyl, 1-acetylaminoethyl, 2-propionylaminoethyl, 3-isopropionylaminopropyl, 4-butyrylaminobutyl, 5-pentanoylaminopentyl, 6-hexanoylaminohexyl, formylaminomethyl, and the like.

The "anilinocarbonyl having optionally a lower alkyl substituent on the phenyl ring" includes an anilinocarbonyl group having optionally 1 to 3 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms on the phenyl ring, for example, anilinocarbonyl, 2-methylanilinocarbonyl, 3-methylanilinocarbonyl, 4-methylanilinocarbonyl, 2-ethylanilinocarbonyl, 3-ethylanilinocarbonyl, 4-ethylanilinocarbonyl, 4-isopropylanilinocarbonyl, 3-butylanilinocarbonyl, 4-pentylanilinocarbonyl, 4-hexylanilinocarbonyl, 3,4-dimethyl-

anilinocarbonyl, 3,4-diethylanilinocarbonyl, 2,4-dimethylanilinocarbonyl, 2,5-dimethylanilinocarbonyl, 2,6-dimethylanilinocarbonyl, 3,4,5-trimethylanilinocarbonyl, and the like.

The "phenylsulfonyl which has optionally a substituent selected from a halogen and a lower alkyl on the phenyl ring" includes a phenylsulfonyl group which has optionally 1 to 3 substitutents selected from a straight chain or branched chain alkyl group having 1 to 6 carbon atoms and a halogen atom, for example, phenylsulfonyl, 2-chlorophenylsulfonyl, 3-chlorophenylsulfonyl, 4-chlorophenylsulfonyl, 2-fluorophenylsulfonyl, 3-fluorophenylsulfonyl, 4-fluorophenylsulfonyl, 2-bromophenylsulfonyl, 3-bromophenylsulfonyl, 4-bromophenylsulfonyl, 2-iodophenylsulfonyl, 3-iodophenylsulfonyl, 4-iodophenylsulfonyl, 3,4-dichlorophenylsulfonyl, 3,5-dichlorophenylsulfonyl, 2,6-dichlorophenylsulfonyl, 2,3-dichlorophenylsulfonyl, 2,4-dichlorophenylsulfonyl, 3,4-difluorophenylsulfonyl, 3,5-dibromophenylsulfonyl, 3,4,5-trichlorophenylsulfonyl, 2-ethyl-3-chlorophenylsulfonyl, 2-methylphenylsulfonyl, 3-methylphenylsulfonyl, 4-methylphenylsulfonyl, 2-ethylphenylsulfonyl, 3-ethylphenylsulfonyl, 4-ethylphenylsulfonyl, 4-isopropylphenylsulfonyl, 3-butylphenylsulfonyl, 4-pentylphenylsulfonyl, 4-hexylphenylsulfonyl, 3,4-dimethylphenylsulfonyl, 3,4-diethylphenylsulfonyl, 2,4-dimethylphenylsulfonyl, 2,5-dimethylphenylsulfonyl, 2,6-dimethylphenylsulfonyl, 3,4,6-trimethylphenylsulfonyl, 3,4,5-trimethylphenylsulfonyl, 3-chloro-4-methylphenylsulfonyl, 4-methyl-5-iodophenylsulfonyl, 3,4-dimethyl-5-bromophenylsulfonyl, 3,5-diiodo-4-methylphenylsulfonyl,

and the like.

The "phthalimido-substituted lower alkyl" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by phthalimido group, for example, phthalimidomethyl, 2-phthalimidoethyl, 1-phthalimidoethyl, 3-phthalimidopropyl, 4-phthalimidobutyl, 5-phthalimidopentyl, 6-phthalimidohexyl, 1,1-dimethyl-2-phthalimidoethyl, 2-methyl-3-phthalimidopropyl, and the like.

The "lower alkynyl" includes a straight chain or branched chain alkynyl having 2 to 6 carbon atoms, for example, ethynyl, 2-propynyl, 2-butynyl, 3-butynyl, 1-methyl-2-propynyl, 2-pentynyl, 2-hexynyl, and the like.

The "benzoyl which has optionally a halogen substituent on the phenyl ring" includes a benzoyl group which has optionally 1 to 3 substituents of a halogen atom on the phenyl ring, for example, benzoyl, 2-chlorobenzoyl, 3-chlorobenzoyl, 4-chlorobenzoyl, 2-fluorobenzoyl, 3-fluorobenzoyl, 4-fluorobenzoyl, 2-bromobenzoyl, 3-bromobenzoyl, 4-bromobenzoyl, 2-iodobenzoyl, 3-iodobenzoyl, 4-iodobenzoyl, 3,4-dichlorobenzoyl, 3,5-dichlorobenzoyl, 2,6-dichlorobenzoyl, 2,3-dichlorobenzoyl, 2,4-dichlorobenzoyl, 3,4-difluorobenzoyl, 3,5-dibromobenzoyl, 3,4,5-trichlorobenzoyl, and the like.

The "phenyl-lower alkoxy" includes a phenylalkoxy group wherein the alkoxy moiety is a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms, for

example, benzyloxy, 2-phenylethoxy, 1-phenylethoxy, 3-phenylpropoxy, 4-phenylbutoxy, 5-phenylpentyloxy, 6-phenylhexyloxy, 1,1-dimethyl-2-phenylethoxy, 2-methyl-3-phenylpropoxy, and the like.

The "amino-lower alkoxy having optionally a substituent selected from a lower alkyl and a lower alkanoyl" include a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms which is substituted by an amino group having optionally 1 to 2 substituents selected from a straight chain or branched chain alkyl group having 1 to 6 carbon atoms and a straight chain or branched chain alkanoyl group having 1 to 6 carbon atoms, for example, aminomethoxy, 2-aminoethoxy, 1-aminoethoxy, 3-aminopropoxy, 4-aminobutoxy, 5-aminopentyloxy, 6-aminohexyloxy, 1,1-dimethyl-2-aminoethoxy, 2-methyl-3-aminopropoxy, acetylaminomethoxy, 1-acetylaminoethoxy, 2-propionylaminoethoxy, 3-isopropionylaminopropoxy, 4-butyrylaminobutoxy, 5-pentanoylaminopentyloxy, 6-hexanoylaminohexyloxy, formylaminomethoxy, methylaminomethoxy, 1-ethylaminoethoxy, 2-propylaminoethoxy, 3-isopropylaminopropoxy, 4-butylaminobutoxy, 5-pentylaminopentyloxy, 6-hexylaminohexyloxy, dimethylaminomethoxy, (N-ethyl-N-propylamino)methoxy, 2-(N-methyl-N-hexylamino)ethoxy, and the like.

The "benzoyloxy which has optionally a halogen substituent on the phenyl ring" includes a benzoyloxy group which has optionally 1 to 3 substituents of a halogen atom on the phenyl ring, for example, benzoyloxy, 2-chloro-

benzoyloxy, 3-chlorobenzoyloxy, 4-chlorobenzoyloxy, 2-fluorobenzoyloxy, 3-fluorobenzoyloxy, 4-fluorobenzoyloxy, 2-bromobenzoyloxy, 3-bromobenzoyloxy, 4-bromobenzoyloxy, 2-iodobenzoyloxy, 3-iodobenzoyloxy, 4-iodobenzoyloxy, 3,4-dichlorobenzoyloxy, 3,5-dichlorobenzoyloxy, 2,6-dichloro-benzoyloxy, 2,3-dichlorobenzoyloxy, 2,4-dichlorobenzoyloxy, 3,4-difluorobenzoyloxy, 3,5-dibromobenzoyloxy, 3,4,5-trichlorobenzoyloxy, and the like.

The "lower alkanoyloxy-substituted lower alkyl" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by a straight chain or branched chain alkanoyloxy group having 2 to 6 carbon atoms, for example, acetyloxymethyl, 2-propion-yloxyethyl, 1-butyryloxyethyl, 3-acetyloxypropyl, 4-acetyl-oxybutyl, 4-isobutyryloxybutyl, 5-pentanoyloxypentyl, 6-acetyloxyhexyl, 6-tert-butylcarbonyloxyhexyl, 1,1-dimethyl-2-hexanoyloxyethyl, 2-methyl-3-acetyloxypropyl, and the like.

The "lower alkylsulfonyloxy-lower alkyl" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by a straight chain or branched chain alkylsulfonyloxy group having 1 to 6 carbon atoms, for example, methylsulfonyloxymethyl, 1-ethyl-sulfonyloxyethyl, 2-propylsulfonyloxyethyl, 3-isopropyl-sulfonyloxypropyl, 4-butylsulfonyloxybutyl, 5-pentylsulfoyl-oxypentyl, 6-hexylsulfonyloxyhexyl, 1,1-dimethyl-2-methyl-sulfoyloxyethyl, 2-methyl-3-ethylsulfonyloxypropyl, and the

like.

The "azido-lower alkyl" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by an azido group, for example, azidomethyl, 1-azidoethyl, 2-azidoethyl, 3-azidopropyl, 4-azidobutyl, 5-azidopentyl, 6-azidohexyl, 1,1-dimethyl-2-azidoethyl, 2-methyl-3-azidopropyl, and the like.

The "lower alkanoyloxyimino" includes a straight chain or branched chain alkanoyloxyimino group having 1 to 6 carbon atoms, for example, formyloxyimino, acetyloxyimino, propionyloxyimino, butyryloxyimino, isobutyryloxyimino, pentanoyloxyimino, tert-butylcarbonyloxyimino, hexanoyl-oxyimino, and the like.

The "lower alkylidene" includes a straight chain or branched chain alkylidene group having 1 to 6 carbon atoms, for example, methylidene, ethylidene, propylidene, isopropylidene, butylidene, pentylidene, hexylidene, and the like.

The "oxiranyl-substituted lower alkyl" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by oxiranyl group, for example, oxiranylmethyl, 1-oxiranylethyl, 2-oxiranylethyl, 3-oxiranylpropyl, 4-oxiranylbutyl, 5-oxiranylpentyl, 6-oxiranylhexyl, 1,1-dimethyl-2-oxiranylethyl, 2-methyl-3-oxiranylpropyl, and the like.

The "lower alkyl having 1 to 2 substituents selected from a lower alkoxy, hydroxy and an amino having

optionally a lower alkyl substituent" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms and having 1 to 2 substituents selected from a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms, hydroxy and an amino having optionally a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, methoxymethyl, 1-ethoxyethyl, 2-propoxyethyl, 3-isopropoxypropyl, 4-butoxybutyl, 5-pentyloxypentyl, 6-hexyloxyhexyl, 1,1-dimethyl-2-methoxyethyl, 2-methyl-3-ethoxypropyl, 3-methoxy-2-hydroxypropyl, hydroxymethyl, 2-hydroxyethyl, 1-hydroxyethyl, 3-hydroxypropyl, 2,3-dihydroxyethyl, 4-hydroxybutyl, 3,4-dihydroxybutyl, 1,1-dimethyl-2-hydroxyethyl, 5,6-dihydroxyhexyl, 5-hydroxypentyl, 6-hydroxyhexyl, 6-(N-ethyl-N-methylamino)-5-methoxyhexyl, 2-methyl-3-hydroxypropyl, aminomethyl, 1-aminoethyl, 2-aminoethyl, 3-aminopropyl, 4-aminobutyl, 5-aminopentyl, 6-aminohexyl, 1,1-dimethyl-2-aminoethyl, 2-methyl-3-aminopropyl, methylaminomethyl, ethylaminomethy, propylaminomethyl, isopropylaminomethyl, butylaminomethyl, tert-butylaminomethyl, pentylaminomethyl, hexylaminomethyl, dimethylaminomethyl, diethylaminomethyl, dipropylaminomethyl, dibutylaminomethyl, dipentylaminomethyl, dihexylaminomethyl, N-methyl-N-ethylaminomethyl, N-methyl-N-propylaminomethyl, N-methyl-N-butylaminomethyl, N-methyl-N-hexylaminomethyl, 1-methylaminoethyl, 2-ethylaminoethyl, 3-propylaminopropyl, 4-butylaminobutyl, 1,1-dimethyl-2-pentylaminoethyl, 5-hexylaminopentyl, 6-dimethylaminohexyl, 4-

dimethylaminobutyl, 2-diethylaminoethyl, 1-(N-methyl-N-hexylamino)ethyl, 3-dihexylaminopropyl, 6-diethylaminohexyl, 4-dibutylaminobutyl, 2-(N-methyl-N-pentylamino)ethyl, 2-hydroxy-3-diethylaminopropyl, 3-hydroxy-4-methylaminobutyl, 5-hydroxy-6-diethylaminohexyl, 4-hydroxy-5-dimethylamino-pentyl, 4-hydroxy-5-methylaminopentyl, 4-hydroxy-5-diethyl-aminopentyl, 5-hydroxy-6-ethylaminohexyl, 5-hydroxy-6-isopropylaminohexyl, 5-hydroxy-6-aminohexyl, and the like.

The "aminocarbonyloxy having optionally a lower alkyl substituent" includes an aminocarbonyloxy group having optionally 1 to 2 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, aminocarbonyloxy, methylaminocarbonyloxy, ethylaminocarbonyloxy, propylamino-carbonyloxy, isopropylaminocarbonyloxy, butylaminocarbonyloxy, tert-butylaminocarbonyloxy, pentylaminocarbonyloxy, hexylamino-carbonyloxy, dimethylaminocarbonyloxy, diethylaminocarbonyloxy, dipropylaminocarbonyloxy, dibutylaminocarbonyloxy, dipentylamino-carbonyloxy, dihexylaminocarbonyloxy, N-methyl-N-ethylamino-carbonyloxy, N-ethyl-N-propylaminocarbonyloxy, N-methyl-N-butyl-aminocarbonyloxy, N-methyl-N-hexylaminocarbonyloxy, and the like.

The "lower alkanoyloxy having optionally a halogen substituent" includes a straight chain or branched chain alkanoyloxy group having 1 to 6 carbon atoms which has optionally 1 to 3 substituents of a halogen atom, for example, in addition to the above lower alkanoyl group, 2,2,2-trifluoroacetyloxy, 2,2,2-trichloroacetyloxy, 2-chloroacetyloxy, 2-bromoacetyloxy, 2-fluoroacetyloxy, 2-iodoacetyloxy, 2,2-difluoroacetyloxy, 2,2-

dibromoacetyloxy, 3,3,3-trifluoropropionyloxy, 3,3,3-trichloropropionyloxy, 3-chloropropionyloxy, 2,3-dichloropropionyloxy, 4,4,4-trichlorobutyryloxy, 4-fluorobutyryloxy, 5-chloropentanoyloxy, 3-chloro-2-methylpropionyloxy, 6-bromohexanoyloxy, 5,6-dibromohexanoyloxy, and the like.

The "amino-lower alkyl having optionally a substituent selected from a lower alkyl and a lower alkanoyl" include a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by an amino group having optionally 1 to 2 substituents selected from a straight chain or branched chain alkyl group having 1 to 6 carbon atoms and a straight chain or branched chain alkanoyl group having 1 to 6 carbon atoms, for example, aminomethyl, 2-aminoethyl, 1-aminoethyl, 3-aminopropyl, 4-aminobutyl, 5-aminopentyl, 6-aminohexyl, 1,1-dimethyl-2-aminoethyl, 2-methyl-3-aminopropyl, acetylaminomethyl, 1-acetylaminoethyl, 2-propionylaminoethyl, 3-isopropionylaminopropyl, 4-butyrylaminobutyl, 5-pentanoylaminopentyl, 6-hexanoylaminohexyl, formylaminomethyl, methylaminomethyl, 1-ethylaminoethyl, 2-propylaminoethyl, 3-isopropylaminopropyl, 4-butylaminobutyl, 5-pentylaminopentyl, 6-hexylaminohexyl, dimethylaminomethyl, (N-ethyl-N-propylamino)methyl, 2-(N-methyl-N-hexylamino)ethyl, and the like.

The "amino-lower alkanoyloxy having optionally a lower alkyl substituent" includes a straight chain or branched chain alkanoyloxy having 2 to 6 carbon atoms which is substituted by an amino group having optionally 1 to 2 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms,

for example, 2-aminoacetyloxy, 3-aminopropionyloxy, 2-aminopropionyloxy, 4-aminobutyryloxy, 5-aminopentanoyloxy, 6-aminohexanoyloxy, 2,2-dimethyl-3-aminopropionyloxy, 2-methyl-3-aminopropionyloxy, 2-methylaminoacetyloxy, 2-ethylaminopropionyloxy, 3-propylaminopropionyloxy, 3-isopropylaminopropionyloxy, 4-butylaminobutyryloxy, 5-pentylaminopentanoyloxy, 6-hexylaminohexanoyloxy, 2-dimethylaminoacetyloxy, 2-diethylaminoacetyloxy, 2-(N-ethyl-N-propylamino)acetyloxy, 3-(N-methyl-N-hexylamino)-propionyloxy, and the like.

The "pyridyl-lower alkyl" include a pyridylalkyl group wherein the alkyl moiety is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, (4-pyridyl)-methyl, 1-(3-pyridyl)ethyl, 2-(2-pyridyl)ethyl, 3-(2-pyridyl)-propyl, 4-(3-pyridyl)butyl, 5-(4-pyridyl)pentyl, 6-(2-pyridyl)-hexyl, 1,1-dimethyl-2-(3-pyridyl)ethyl, 2-methyl-3-(4-pyridyl)-propyl, and the like.

The "5- or 6-membered saturated heterocyclic group which is formed by binding the groups R^{82} and R^{83} together with the nitrogen atom to which they bond with or without being intervened with nitrogen, oxygen or sulfur atom" includes, for example, pyrrolidinyl, piperidinyl, piperazinyl, morpholino, thiomorpholino, and the like.

The above heterocyclic group which has a substituent selected from oxo, a lower alkyl, a lower alkanoyl and carbamoyl includes the above heterocyclic groups which have 1 to 3 substituents selected from oxo, a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, a straight chain or

branched chain alkanoyl group having 1 to 6 carbon atoms, and carbamoyl group, for example, 4-methylpiperazinyl, 3,4-dimethylpiperazinyl, 3-ethylpyrrolidinyl, 2-propylpyrrolidinyl, 3,4,5-trimethylpiperidinyl, 4-butylpiperidinyl, 3-pentylmorpholino, 4-hexylpiperazinyl, 2-methylthiomorpholino, 4-acetylpiperazinyl, 2-propionylmorpholino, 3-butyrylthiomorpholino, 3-pentanoylpyrrolidinyl, 4-hexanoylpiperidinyl, 3-methyl-4-acetylpiperazinyl, 2-carbamoylpyrrolidinyl, 4-carbamoylpiperazinyl, 3-carbamoylthiomorpholino, 2-carbamoylmorpholino, 3-carbamoylpiperidinyl, 1-oxo-thiomorpholino, 1,1-dioxothiomorpholino, and the like.

The "lower alkylsulfonyl" includes a straight chain or branched chain alkylsulfonyl group having 1 to 6 carbon atoms, for example, methylsulfonyl, ethylsulfonyl, propylsulfonyl, isopropylsulfonyl, butylsulfonyl, tert-butylsulfonyl, pentylsulfonyl, hexylsulfonyl, and the like.

The "aminocarbonyl having optionally a lower alkyl substituent" includes an aminocarbonyl group having optionally 1 to 2 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, aminocarbonyl, methylaminocarbonyl, ethylaminocarbonyl, propylaminocarbonyl, isopropylaminocarbonyl, butylaminocarbonyl, tert-butylaminocarbonyl, pentylaminocarbonyl, hexylaminocarbonyl, dimethylaminocarbonyl, diethylaminocarbonyl, dipropylaminocarbonyl, dibutylaminocarbonyl, dipentylaminocarbonyl, dihexylaminocarbonyl, N-methyl-N-ethylaminocarbonyl, N-ethyl-N-propylaminocarbonyl, N-methyl-N-butylaminocarbonyl, N-methyl-N-hexylaminocarbonyl, and the like.

The "cyano-substituted lower alkyl" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by cyano group, for example, cyanomethyl, 2-cyanoethyl, 1-cyanoethyl, 3-cyanopropyl, 4-cyanobutyl, 5-cyanopentyl, 6-cyanohexyl, 1,1-dimethyl-2-caynoethyl, 2-methyl-3-cyanopropyl, and the like.

The "lower alkoxycarbonyl-substituted lower alkyl" includes an alkoxycarbonyl-substituted straight chain or branched chain alkyl group having 1 to 6 carbon atoms wherein the alkoxycarbonyl moiety is a straight chain or branched chain alkoxycarbonyl group having 1 to 6 carbon atoms, for example, methoxycarbonylmethyl, 3-methoxycarbonylpropyl, ethoxycarboxymethyl, 3-ethoxycarbonylpropyl, 4-ethoxycarbonylbutyl, 5-isopropoxycarbonylpentyl, 6-propoxycarbonylhexyl, 1,1-dimethyl-2-butoxycarbonylethyl, 2-methyl-3-tert-butoxycarbonylpropyl, 2-pentyloxycarbonylethyl, hexyloxycarbonylmethyl, and the like.

The "carboxy-substituted lower alkyl" includes a carboxy-substituted alkyl group wherein the alkyl moiety is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, carboxymethyl, 2-carboxyethyl, 1-carboxyethyl, 3-carboxypropyl, 4-carboxybutyl, 5-carboxypentyl, 6-carboxyhexyl, 1,1-dimethyl-2-carboxyethyl, 2-methyl-3-carboxypropyl, and the like.

The "tetrahydropyranyloxy-substituted lower alkyl" includes a tetrahydropyranyloxy-substituted straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, (2-tetrahydropyranyloxy)methyl, 2-(3-tetrahydropyranyl-

oxy)ethyl, 1-(4-tetrahydropyranyloxy)ethyl, 3-(2-tetrahydropyranyloxy)propyl, 4-(3-tetrahydropyranyloxy)butyl, 5-(4-tetrahydropyranyloxy)pentyl, 6-(2-tetrahydropyranyloxy)hexyl, 1,1-dimethyl-2-(3-tetrahydropyranyloxy)ethyl, 2-methyl-3-(4-tetrahydropyranyloxy)propyl, and the like.

The "piperidinyl having optionally a phenyl-lower alkyl substituent" includes a piperidinyl which has optionally a substituent of a phenylalkyl group wherein the alkyl moiety is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, piperidinyl, 1-benzyl-4-piperidinyl, 1-(2-phenylethyl)-3-piperidinyl, 1-(1-phenylethyl)-2-piperidinyl, 1-(3-phenylpropyl)-4-piperidinyl, 1-(4-phenylbutyl)-4-piperidinyl, 1-(5-phenylpentyl)-4-piperidinyl, 1-(6-phenylhexyl)-4-piperidinyl, 1-(1,1-dimethyl-2-phenylethyl)-3-piperidinyl, 1-(2-methyl-3-phenylpropyl)-2-piperidinyl, and the like.

The "imidazolyl-substituted lower alkanoyl" includes an imidazolyl-substituted alkanoyl group wherein the alkanoyl moiety is a straight chain or branched chain alkanoyl group having 2 to 6 carbon atoms, for example, (1-imidazolyl)acetyl, 3-(2-imidazolyl)propionyl, 2-(4-imidazolyl)propionyl, 4-(1-imidazolyl)butyryl, 2,2-dimethyl-3-(2-imidazolyl)propionyl, 5-(4-imidazolyl)-pentanoyl, 6-(1-imidazolyl)hexanoyl, and the like.

The "amino-lower alkanoyl having optionally a substituent selected from a lower alkyl and a lower alkoxycarbonyl" includes a straight chain or branched chain alkanoyl having 2 to 6 carbon atoms which is substituted by an amino group having optionally 1 to 2 substituents selected from a straight chain or

branched chain alkyl group having 1 to 6 carbon atoms and a straight chain or branched chain alkoxycarbonyl group having 1 to 6 carbon atoms, for example, 2-aminoacetyl, 3-aminopropionyl, 2-aminopropionyl, 4-aminobutyryl, 5-aminopentanoyl, 6-aminohexanoyl, 2,2-dimethyl-3-aminopropionyl, 2-methyl-3-aminopropionyl, 2-methylaminoacetyl, 2-ethylaminopropionyl, 3-propylaminopropionyl, 3-isopropylaminopropionyl, 4-butylaminobutyryl, 5-pentylaminopentanoyl, 6-hexylaminohexanoyl, 2-dimethylaminoacetyl, 2-diethylaminoacetyl, 2-(N-ethyl-N-propylamino)acetyl, 3-(N-methyl-N-hexylamino)propionyl, 2-methoxycarbonylaminoacetyl, 2-ethoxycarbonylaminoacetyl, 3-propoxycarbonylaminopropionyl, 4-butoxycarbonylaminobutyryl, 2-tert-butoxycarbonylaminoacetyl, 5-pentyloxycarbonylaminopentanoyl, 6-hexyloxycarbonylaminohexanoyl, 2-(N-methyl-N-tert-butoxycarbonylamino)acetyl, and the like.

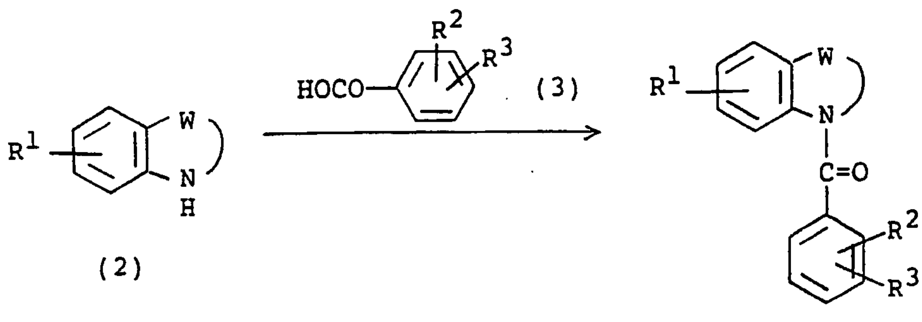
The "aminocarbonyl-lower alkyl having a lower alkyl substituent" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by an aminocarbonyl group having 1 to 2 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, methylaminocarbonylmethyl, 1-ethylaminocarbonylethyl, 2-propylaminocarbonylethyl, 3-isopropylaminocarbonylpropyl, 4-butylaminocarbonylbutyl, 5-pentylaminocarbonylpentyl, 6-hexylaminocarbonylhexyl, dimethylaminocarbonylmethyl, 3-diethylaminocarbonylpropyl, diethylaminocarbonylmethyl, (N-ethyl-N-propylamino)carbonylmethyl, 2-(N-

methyl-N-hexylamino)carbonylethyl, and the like.

The "amino-substituted lower alkoxy having optionally a lower alkyl substituent" includes an amino-substituted straight chain or branched chain alkoxy having 1 to 6 carbon atoms which has optionally 1 to 2 substituents of a straight chain or branched chain alkyl having 1 to 6 carbon atoms, such as aminomethoxy, 2-aminoethoxy, 1-aminoethoxy, 3-aminopropoxy, 4-aminobutoxy, 5-aminopentyloxy, 6-aminohexyloxy, 1,1-dimethyl-2-aminoethoxy, 2-methyl-3-aminopropoxy, methylaminomethoxy, 1-ethylaminoethoxy, 2-propylaminoethoxy, 3-isopropylaminopropoxy, 4-butylaminobutoxy, 5-pentylaminopentyloxy, 6-hexylaminohexyloxy, dimethylaminomethoxy, (N-ethyl-N-propylamino)methoxy, 2-(N-methyl-N-hexylamino)ethoxy, and the like.

The compounds of the present invention can be prepared by various processes, for example, by the processes shown in the following reaction schemes.

[Reaction Scheme-1]



(2)

(1)

wherein R^1, R^2, R^3, and W are the same as defined above.

The process of Reaction Scheme-1 is carried out by

reacting a benzoheterocyclic compound of the formula (2) and a carboxylic acid compound of the formula (3) by a conventional amido bond forming reaction. The amido bond forming reaction can be carried out under the conditions for the conventional amido bond forming reaction, for example,

(a) a mixed acid anhydride process, i.e. a process of reacting the carboxylic acid compound (3) with an alkyl-halocarboxylic acid to form a mixed acid anhydride and reacting the resultant with the amine compound (2),

(b) an activated ester process, i.e. a process of converting the carboxylic acid compound (3) into an activated ester, such as p-nitrophenyl ester, N-hydroxy-succinimide ester, 1-hydroxybenzotriazole ester, etc., and reacting the resultant with the amine compound (2),

(c) a carbodiimide process, i.e. a process of condensing the carboxylic acid compound (3) and the amine compound (2) in the presence of an activating agent such as dicyclohexylcarbodiimide, carbonyldiimidazole, etc.,

(d) other processes, i.e. a process of converting the carboxylic acid compound (3) into a carboxylic anhydride by treatment with a dehydrating agent such as acetic anhydride, and reacting the resultant with the amine compound (2); a process of reacting an ester of the carboxylic acid compound (3) with a lower alcohol and the amine compound (2) at a high temperature under high pressure; a process of reacting an acid halide compound of the carboxylic acid compound (3), i.e. a carboxylic acid

halide, with the amine compound (2), and the like.

The mixed acid anhydride used in the above mixed acid anhydride process (a) is obtained by the known Schötten-Baumann reaction, and the reaction product is used without isolation from the reaction mixture for the reaction with the amine compound (2) to give the desired compound of the formula (1). The Schötten-Baumann reaction is usually carried out in the presence of a basic compound. The basic compound is any conventional compounds used for the Schötten-Baumann reaction and includes, for example, organic basic compounds such as triethylamine, trimethylamine, pyridine, dimethylaniline, N-methylmorpholine, 1,5-diazabicyclo[4.3.0]nonene-5 (DBN), 1,8-diazabicyclo[5.4.0]-undecene-7 (DBU), 1,4-diazabicyclo[2.2.2]octane (DABCO), etc., and inorganic basic compounds such as potassium carbonate, sodium carbonate, potassium hydrogen carbonate, sodium hydrogen carbonate, etc. The reaction is usually carried out at a temperature of from about -20°C to about 100°C, preferably from about 0°C to about 50°C, for about 5 minutes to about 10 hours, preferably about 5 minutes to about 2 hours.

The reaction of the thus obtained mixed acid anhydride with the amine compound (2) is usually carried out at a temperature of from about -20°C to about 150°C, preferably about 10°C to about 50°C, for about 5 minutes to about 10 hours, preferably about 5 minutes to about 5 hours. The mixed acid anhydride process is usually carried

out in an appropriate solvent. The solvent is any conventional solvents which are usually used in the mixed acid anhydride process and includes, for example, halogenated hydrocarbons (e.g. chloroform, dichloromethane dichloroethane, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), ethers (e.g. diethyl ether, diisopropyl ether, tetrahydrofuran, dimethoxyethane, etc.), esters (e.g. methyl acetate, ethyl acetate, etc.), aprotic polar solvents (e.g. N,N-dimethylformamide, dimethylsulfoxide, hexamethylphosphoric triamide, etc.), or a mixture of these solvents. The alkylhalocarboxylic acid used in the mixed acid anhydride process includes, for example, methyl chloroformate, methyl bromoformate, ethyl chloroformate, ethyl bromoformate, isobutyl chloroformate, and the like. In said process, the carboxylic acid compound (3), the alkylhalocarboxylic acid and the amine (2) are usually used in each equimolar amount, but preferably, the alkylhalocarboxylic acid and the carboxylic acid compound (3) are used each in an amount of about 1 to 1.5 mole to 1 mole of the amine (2).

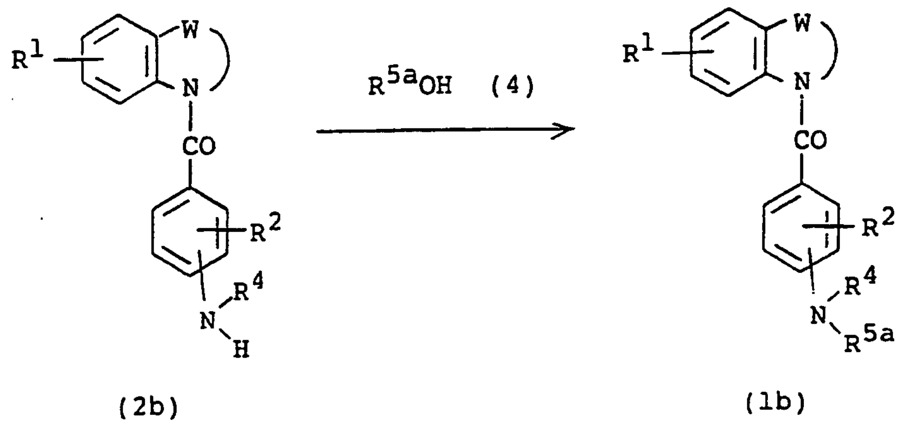
Among the above other processes (d), in case of the process of reacting the carboxylic acid halide with the amine compound (2), the reaction is usually carried out in the presence of a basic compound in an appropriate solvent. The basic compound is any conventional compounds and includes, in addition to the basic compounds used for the above-mentioned Schötten-Baumann reaction, sodium hydroxide,

potassium hydroxide, sodium hydride, potassium hydride. etc. The solvent includes, in addition to the solvents used for the above-mentioned mixed acid anhydride process, alcohols (e.g. methanol, ethanol, propanol, butanol, 3-methoxy-1-butanol, ethylcellosolve, methylcellosolve, etc.), acetonitrile, pyridine, acetone, water, and the like. The amount of the amine compound (2) and the carboxylic acid halide is not critical, but the carboxylic acid halide is usually used at least in equimolar amount, preferably about 1 to 5 moles to 1 mole of the amine compound (2). The reaction is usually carried out at a temperature of from about -20°C to about 180°C, preferably from about 0°C to about 150°C, for about 5 minutes to about 30 hours.

The amido bond forming reaction in the above Reaction Scheme-1 may also be carried out by reacting the carboxylic acid compound (3) and the amine (2) in the presence of a condensation agent, i.e. phosphoric compounds such as triphenylphosphine, diphenylphosphinyl chloride, phenyl-N-phenylphosphoramide chloridate, diethyl chlorophosphate, diethyl phosphorocyanidate, diphenylphosphoric azide, bis(2-oxo-3-oxazolidinyl)phosphinic chloride, etc. The reaction is usually carried out in the presence of the solvent and basic compound as used in the above reaction of the carboxylic acid halide and the amine (2) at a temperature of from about -20°C to about 150°C, preferably about 0°C to about 100°C, for about 5 minutes to about 30 hours. The condensation agent and the carboxylic acid compound (3)

are used at least in equimolar amount, preferably about 1 to 2 moles, to 1 mole of the amine (2).

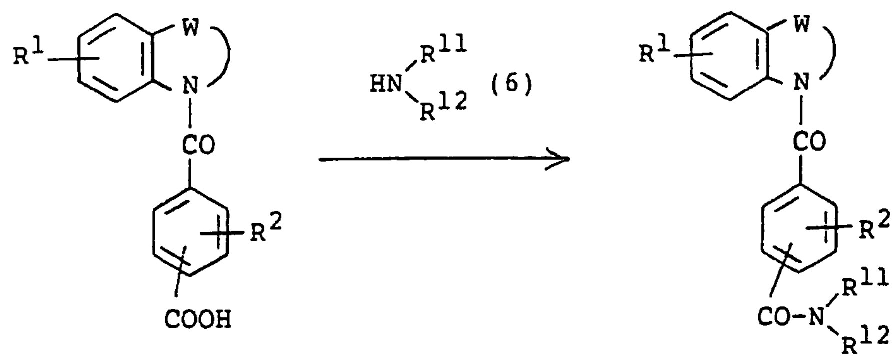
[Reaction Scheme-2]



wherein R^1, R^2, R^4 and W are as defined above, R^{5a} is the same as R^5 as defined above except excluding an anilino-carbonyl having optionally a lower alkyl substituent on the phenyl ring, a phenylsulfonyl having optionally a substituent selected from a halogen atom and a lower alkyl on the phenyl ring and quinolylsulfonyl.

The reaction of the compound (2b) and the compound (4) is carried out in the same manner as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

[Reaction Scheme-3]

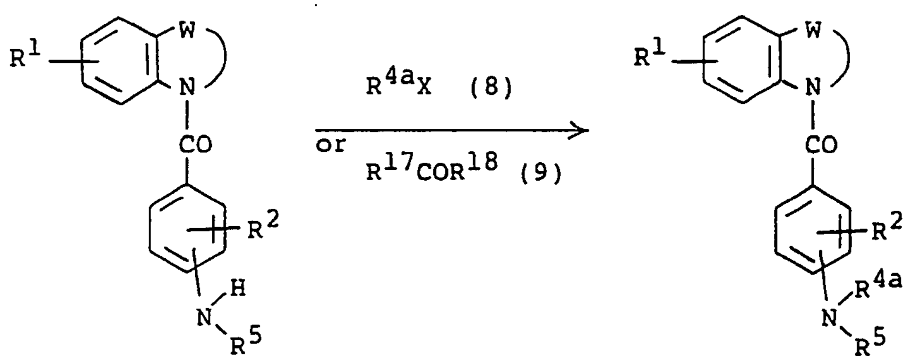


(5) (1c)

wherein R^1, R^2, R^{11}, R^{12} and W are as defined above.

The reaction of the compound (5) and the compound (6) is carried out under the same conditions as used in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

[Reaction Scheme-4]



(7) (1d)

wherein R^1, R^2, R^5 and W are as defined above, and R^{4a} is a lower alkyl, R^{17} and R^{18} are each hydrogen atom or a lower alkyl, and X is a halogen atom.

The reaction of the compound (7) and the compound (8) is usually carried out in an inert solvent in the

presence or absence of a basic compound. The inert solvent includes, for example, aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), ethers (e.g. tetrahydrofuran, dioxane, diethylene glycol dimethyl ether, etc.), halogenated hydrocarbons (e.g. dichloromethane, chloroform, carbon tetrachloride, etc.), lower alcohols (e.g. methanol, ethanol, isopropanol, butanol, tert-butanol, etc.), acetic acid, ethyl acetate, acetone, acetonitrile, pyridine, dimethylsulfoxide, dimethylformamide, hexamethylphosphoric triamide, etc., or a mixture of these solvents. The basic compound includes, for example, carbonates (e.g. sodium carbonate, potassium carbonate, sodium hydrogen carbonate, potassium hydrogen carbonate, etc.), metal hydroxides (e.g. sodium hydroxide, potassium hydroxide, etc.), sodium hydride, potassium, sodium, sodium amide, metal alcoholates (e.g. sodium methoxide, sodium ethoxide, etc.), and organic basic compounds (e.g. pyridine, N-ethyldiisopropylamine, dimethylaminopyridine, triethylamine, 1,5-diazabicyclo-[4.3.0]nonene-(5) (DBN), 1,8-diazabicyclo[5.4.0]undecene-7 (DBU), 1,4-diazabicyclo[2.2.2]octane (DABCO), etc.). The amount of the compound (7) and the compound (8) is not critical, but the compound (8) is usually used at least in equivalent amount, preferably 1 to 10 moles, to 1 mole of the compound (7). The reaction is usually carried out at a temperature of from about 0°C to about 200°C, preferably from about 0°C to about 170°C, for about 30 minutes to about 30 hours. In the reaction, an alkali metal halide (e.g.

sodium iodide, potassium iodide, etc.) may be added to the reaction system.

The reaction of the compound (7) and the compound (9) is carried out in an appropriate solvent or without solvent in the presence of a reducing agent. The solvent includes, for example, water, alcohols (e.g. methanol, ethanol, isopropanol, etc.), acetonitrile, formic acid, acetic acid, ethers (e.g. dioxane, diethyl ether, diglyme, tetrahydrofuran, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), or a mixture of these solvents. The reducing agent includes, for example, formic acid, fatty acid alkali metal salts (e.g. sodium formate, etc.), hydrogenating reducing agents (e.g. sodium boro hydride, sodium cyanoboro hydride, lithium aluminum hydride, etc.), catalystic reducing agents (e.g. palladium black, palladium-carbon, platinum oxide, platinum black, Raney nickel, etc.).

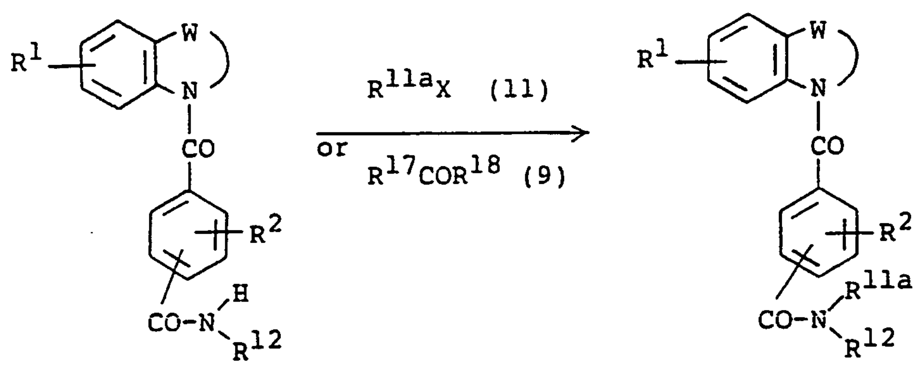
When formic acid is used as the reducing agent, the reaction is usually carried out at a temperature of from room temperature to about 200°C, peferably about 50°C to about 150°C, for about 1 to 10 hours. The formic acid is usually used in a large excess amount to the compound (7).

When a hydrogenating reducing agent is used, the reaction is usually carried out at a temperature of about -30°C to about 100°C, preferably about 0°C to about 70°C, for about 30 minutes to about 12 hours. The reducing agent is usually used in an amount of 1 to 20 moles, preferably 1

to 6 moles, to 1 mole of the compound (7). When lithium aluminum hydride is used as the reducing agent, it is preferable to use a solvent selected from ethers (e.g. diethyl ether, dioxane, tetrahydrofuran, diglyme, etc.) and aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.).

When a catalytic reducing agent is used, the reaction is usually carried out under atmospheric pressure to about 20 atm., preferably atmospheric pressure to about 10 atm. under hydrogen atmosphere or in the presence of a hydrogen donor (e.g. formic acid, ammonium formate, cyclohexene, hydrazine hydrate, etc.) at a temperature of about -30°C to about 100°C, preferably about 0°C to about 60°C, for about 1 to 12 hours. The catalytic reducing agent is usually used in an amount of about 0.1 to 40 % by weight, preferably about 1 to 20 % by weight, of the amount of the compound (7). The compound (9) is usually used at least in equivalent amount, preferably equivalent to a large excess amount, to the compound (7).

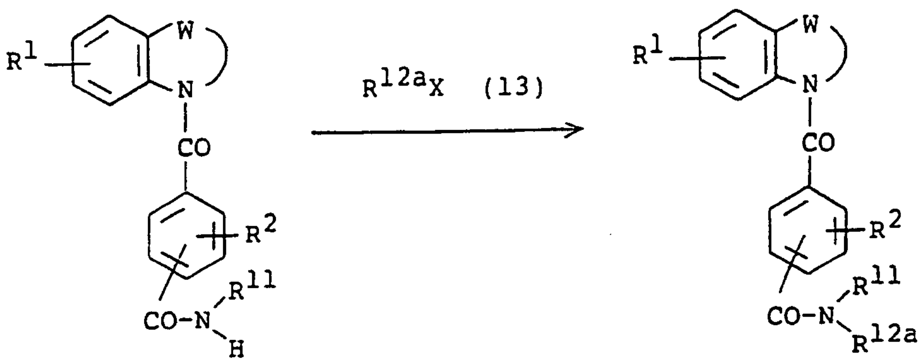
[Reaction Scheme-5A]



(10) (1e)

wherein R^1, R^2, R^{12}, R^{17}, R^{18}, X and W are as defined above, and R^{11a} is a lower alkyl.

[Reaction Scheme-5B]



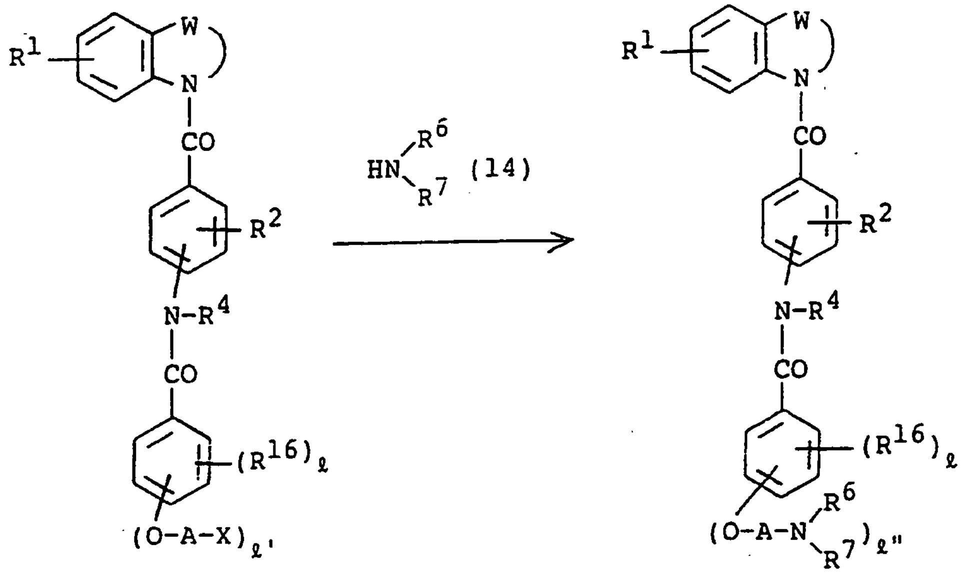
(12) (1f)

wherein R^1, R^2, R^{11}, X and W are as defined above, and R^{12a} is a cycloalkyl.

The reaction of the compound (10) and the compound (11) in the Reaction Scheme-5A and the reaction of the compound (12) and the compound (13) in the Reaction Scheme-5B are carried out in the same manner as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

Besides, the reaction of the compound (10) and the compound (9) in the Reaction Scheme-5A is carried out in the same manner as in the reaction of the compound (7) and the compound (9) in the above Reaction Scheme-4.

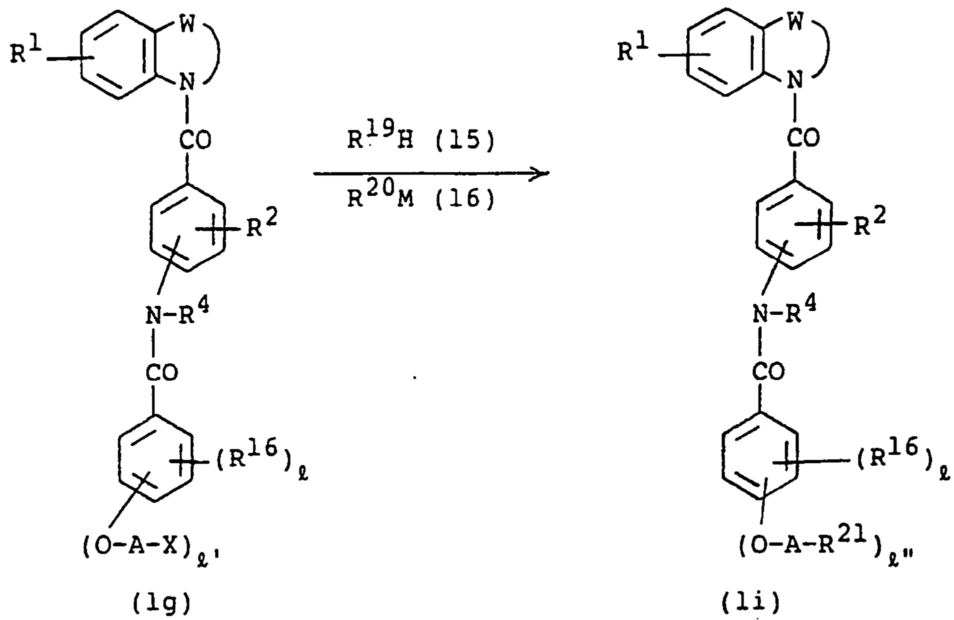
[Reaction Scheme-6A]



(1g) (1h)

wherein R^1, R^2, R^4, R^{16}, R^6, R^7, X, W, and A are as defined above, ℓ is 0 or an integer of 1 to 3, ℓ' and ℓ'' are each an integer of 1 to 3, provided that $\ell + \ell'$ and $\ell + \ell''$ are each an integer not more than 3.

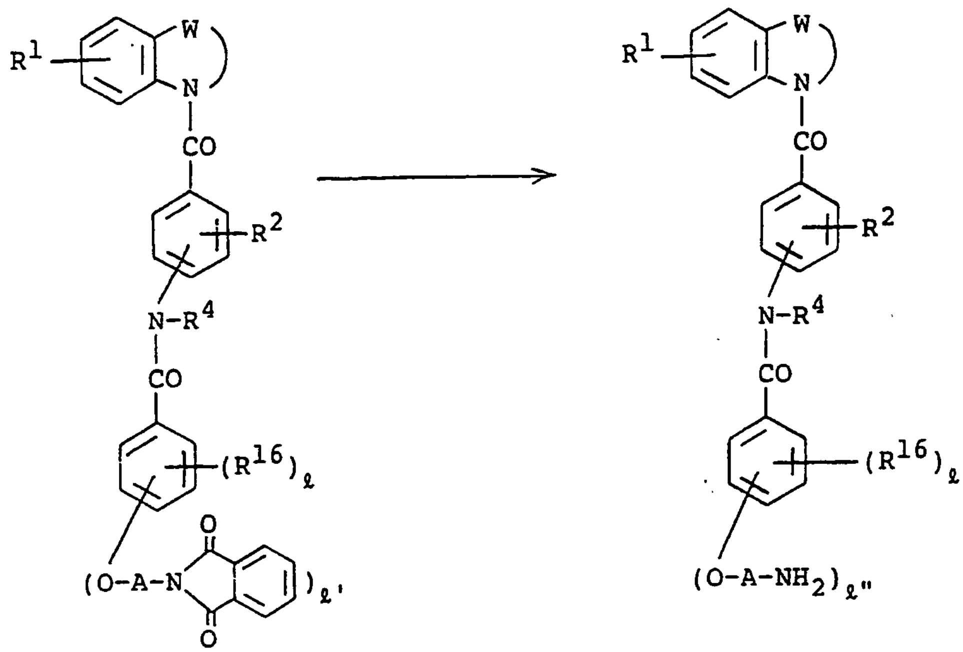
[Reaction Scheme-6B]



wherein R^1, R^2, R^4, R^{16}, X, W, A, ℓ, ℓ', and ℓ'' are as defined above, and R^{19} is a lower alkanoyloxy, R^{20} is a lower alkanoyloxy, hydroxy or phthalimido, R^{21} is the same as as R^{19} and R^{20}, and M is an alkali metal (e.g. potassium, sodium, etc.).

The reaction of the compound (1g) and the compound (14) in the Reaction Scheme-6A and the reaction of the compound (1g) and the compound (15) or (16) in the Reaction Scheme-6B can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4. In the reaction, an alkali metal halide (e.g. sodium iodide, potassium iodide, etc.) may be added to the reaction system.

[Reaction Scheme-7]



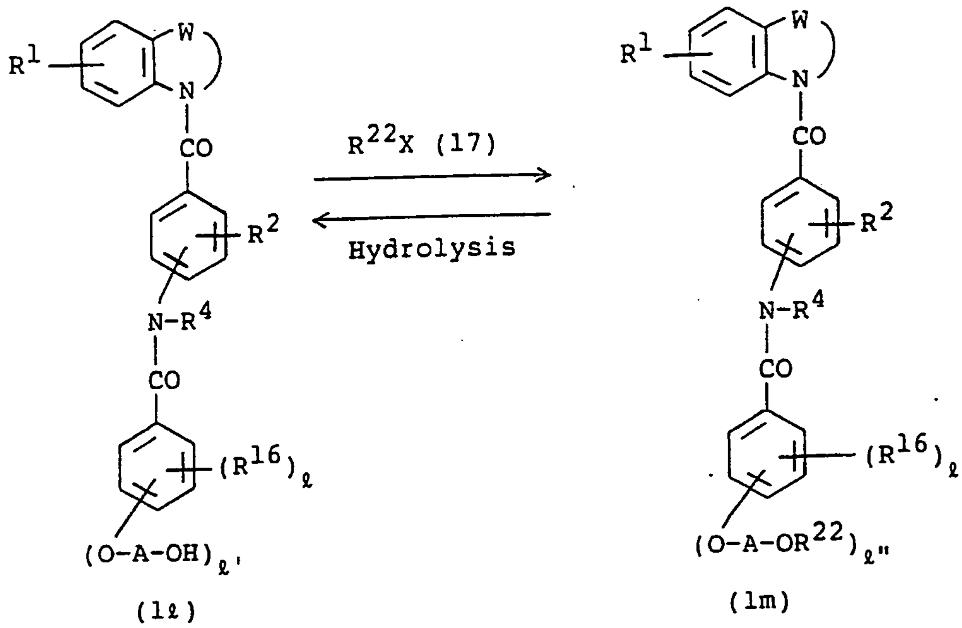
(1j) (1k)

wherein R^1, R^2, R^4, R^{16}, W, ℓ, ℓ', ℓ" and A are as defined above.

The reaction of converting the compound (1j) into the compound (1k) can be carried out by reacting the compound (1j) with hydrazine in an appropriate solvent or by hydrolyzing the compound (1j). The solvent used in the reaction with hydrazine includes water and further the same solvent as used in the reaction of the compound (2b) and the compound (4) in the above Reaction Scheme-2. The reaction is usually carried out at a temperature of from room temperature to about 120°C, preferably about 0°C to about 100°C, for about 0.5 to 5 hours. Hydrazine is usually used in an amount of at least 1 mole, preferably about 1 to 5 moles, to 1 mole of the compound (1j).

The hydrolysis can be carried out in an appropriate solvent or without solvent in the presence of an acid or a basic compound. The solvent includes, for example, water, lower alcohols (e.g. methanol, ethanol, isopropanol, etc.), ketones (e.g. acetone, methyl ethyl ketone, etc.), ethers (e.g. dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, etc.), fatty acids (e.g. acetic acid, formic acid, etc.), or a mixture of these solvents. The acid includes, for example, mineral acids (e.g. hydrochloric acid, sulfuric acid, hydrobromic acid, etc.) and organic acids (e.g. formic acid, acetic acid, aromatic sulfonic acids, etc.). The basic compound includes, for example, metal carbonates (e.g. sodium carbonate, potassium carbonate, etc.), metal hydroxides (e.g. sodium hydroxide, potassium hydroxide, calcium hydroxide, etc.), and the like. The reaction is usually carried out at a temperature of from room temperature to about 200°C, preferably from room temperature to about 150°C, for about 10 minutes to 25 hours.

[Reaction Scheme-8]

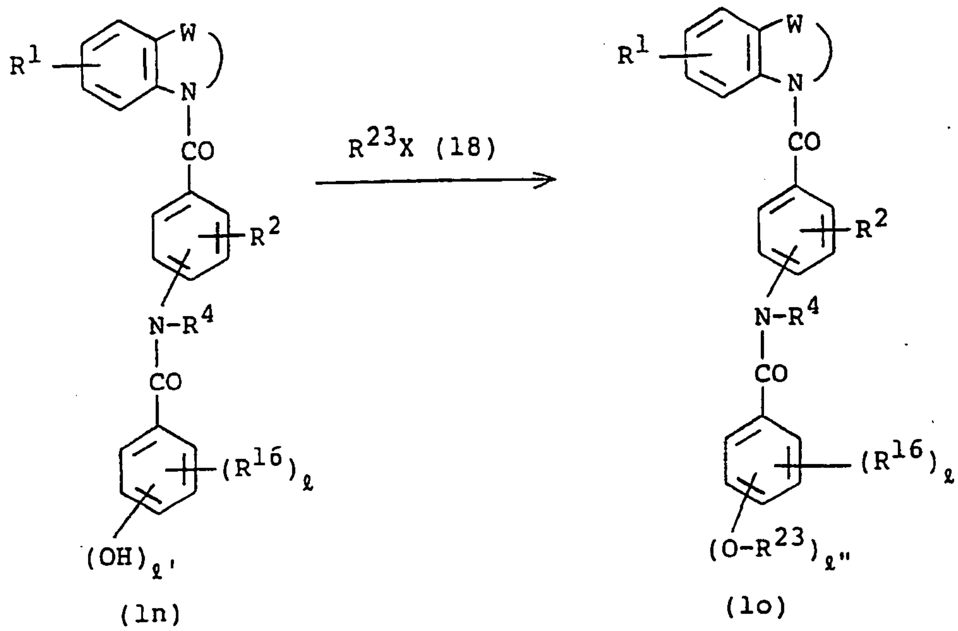


wherein R^1, R^2, R^4, W, R^{16}, ℓ, ℓ', ℓ'', X, and A are as defined above, and R^{22} is a lower alkanoyl.

The reaction of the compound (1ℓ) and the compound (17) is carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the Reaction Scheme-4. In the reaction, an alkali metal halide (e.g. sodium iodide, potassium iodide, etc.) may be added to the reaction system.

The reaction of converting the compound (1m) into the compound (1ℓ) can be carried out under the same condition as in the hydrolysis of the compound (1j) in the Reaction Scheme-7.

[Reaction Scheme-9]

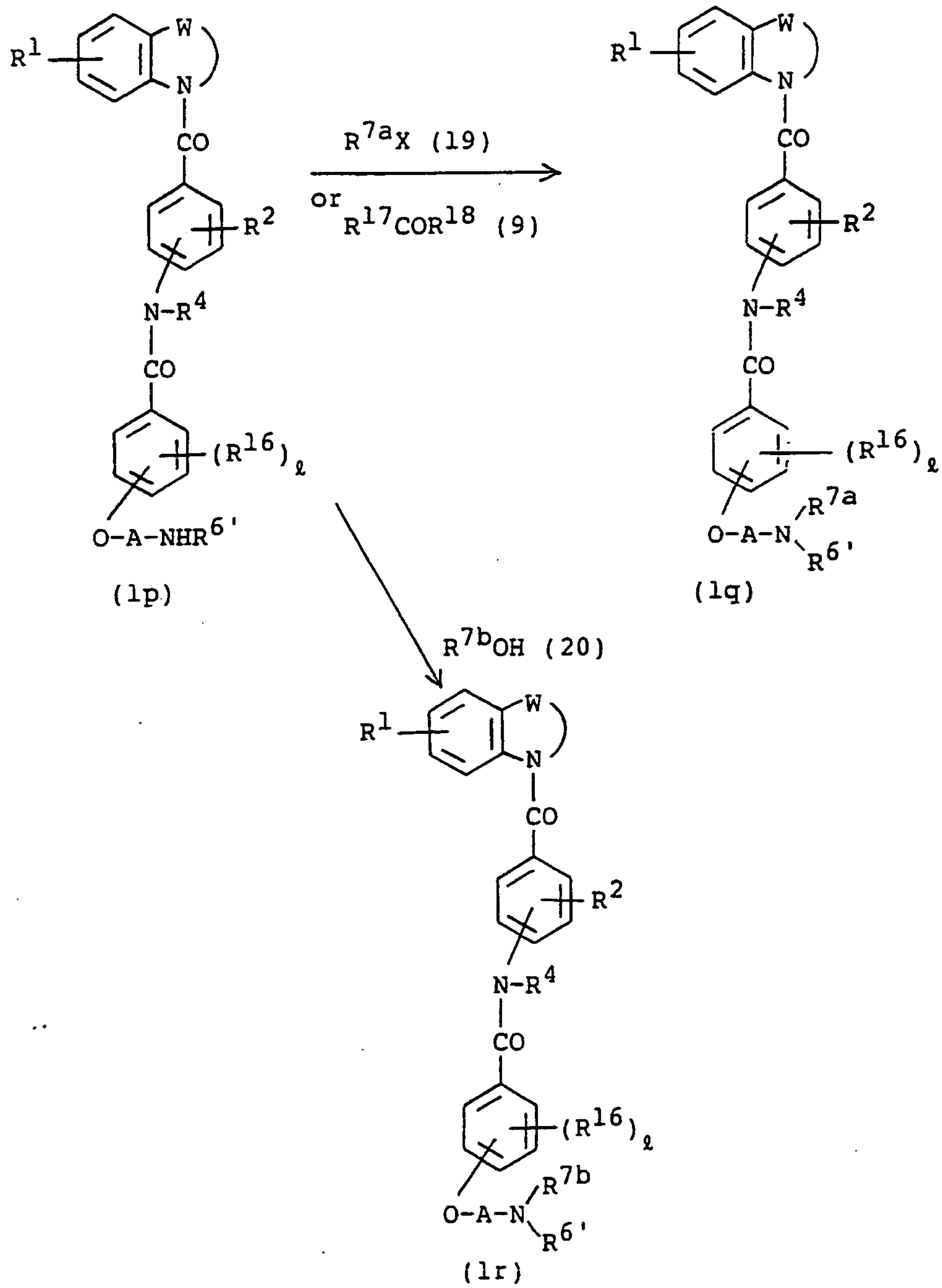


wherein R^1, R^2, R^4, W, R^{16}, ℓ, ℓ', ℓ'', and X are as defined above, and R^{23} is a lower alkyl, a lower alkanoyloxy-substituted lower alkyl, a halogen-substituted lower alkyl, a carboxy-substituted lower alkyl, a carbamoyl-substituted lower alkyl, a hydroxy-substituted lower alkyl, a lower alkoxycarbonyl-substituted lower alkyl, a phthalimido-substituted lower alkyl, an aminocarbonyl-lower alkyl having optionally a lower alkyl substituent, or a group of the formula: $-A-N\begin{matrix}R^6\\R^7\end{matrix}$ (A, R^6 and R^7 are as defined above).

The reaction of the compound (1n) and the compound (18) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4. In the reaction, an alkali metal halide (e.g. sodium iodide, potassium iodide, etc.) may be

added to the reaction system.

[Reaction Scheme-10]



wherein R^1, R^2, R^4, W, R^{16}, R^{17}, R^{18}, ℓ, X, and A are as defined above, and $R^{6'}$ is hydrogen atom, a lower alkyl

having optionally a hydroxy substituent, a lower alkanoyl, or benzoyl, R^{7a} is a lower alkyl having optionally a hydroxy substituent, and R^{7b} is a lower alkanoyl or benzoyl.

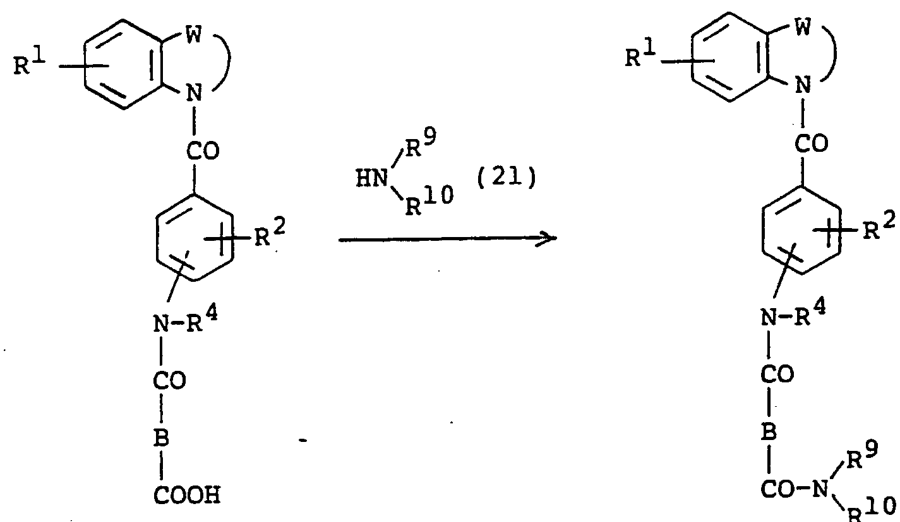
The reaction of the compound (1p) and the compound (19) or the compound (9) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) or the compound (9) in the above Reaction Scheme-4.

The reaction of the compound (1p) and the compound (20) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the Reaction Scheme-1.

Besides, the compound (1r) can also be obtained by reacting the compound (1p) with a compound of the formula: $(R^{7b})_2O$ (R^{7b} is as defined above). The reaction can be carried out in an appropriate solvent or without solvent in the presence or absence, peferably presence, of a basic compound. The solvent includes, for example, the above-mentioned aromatic hydrocarbons, lower alcohols (e.g. methanol, ethanol, propanol, etc.), dimethylformamide, dimethylsulfoxide, and further halogenated hydrocarbons (e.g. chloroform, methylene chloride, etc.), acetone, pyridine, etc. The basic compound includes, for example, tertiary amines (e.g. triethylamine, pyridine, etc.), sodium hydroxide, potassium hydroxide, sodium hydride, and the like. The above reaction can also be carried out in a solvent such as acetic acid or benzoic acid in the presence of a mineral acid (e.g. sulfuric acid, etc.). The acid

anhydride is usually used in an equimolar amount or more, preferably 1 to 10 moles, to 1 mole of the starting compound, and the reaction is usually carried out at a temperature of about 0°C to about 200°C, preferably from about 0°C to about 150°C, for about 0.5 to 15 hours.

[Reaction Scheme-11]

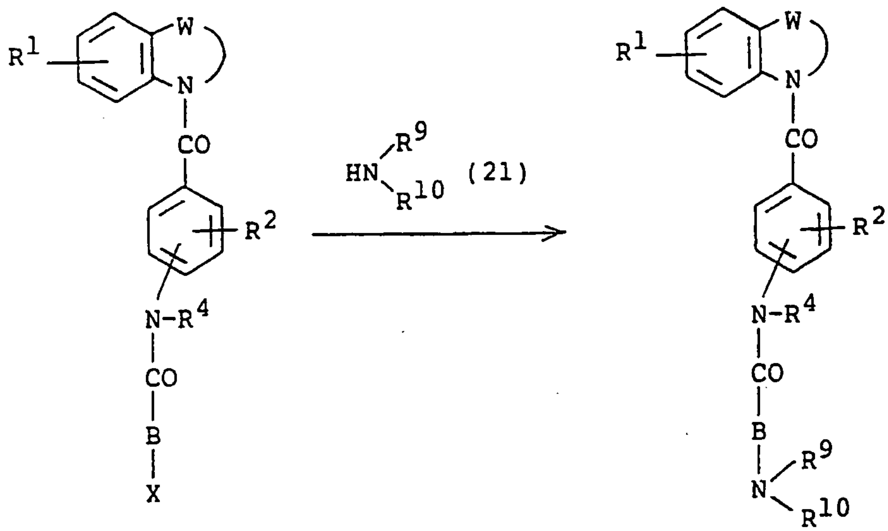


(1s) (1t)

wherein R^1, R^2, R^4, R^9, R^{10}, W, and B are as defined above.

The reaction of the compound (1s) and the compound (21) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

[Reaction Scheme-12]

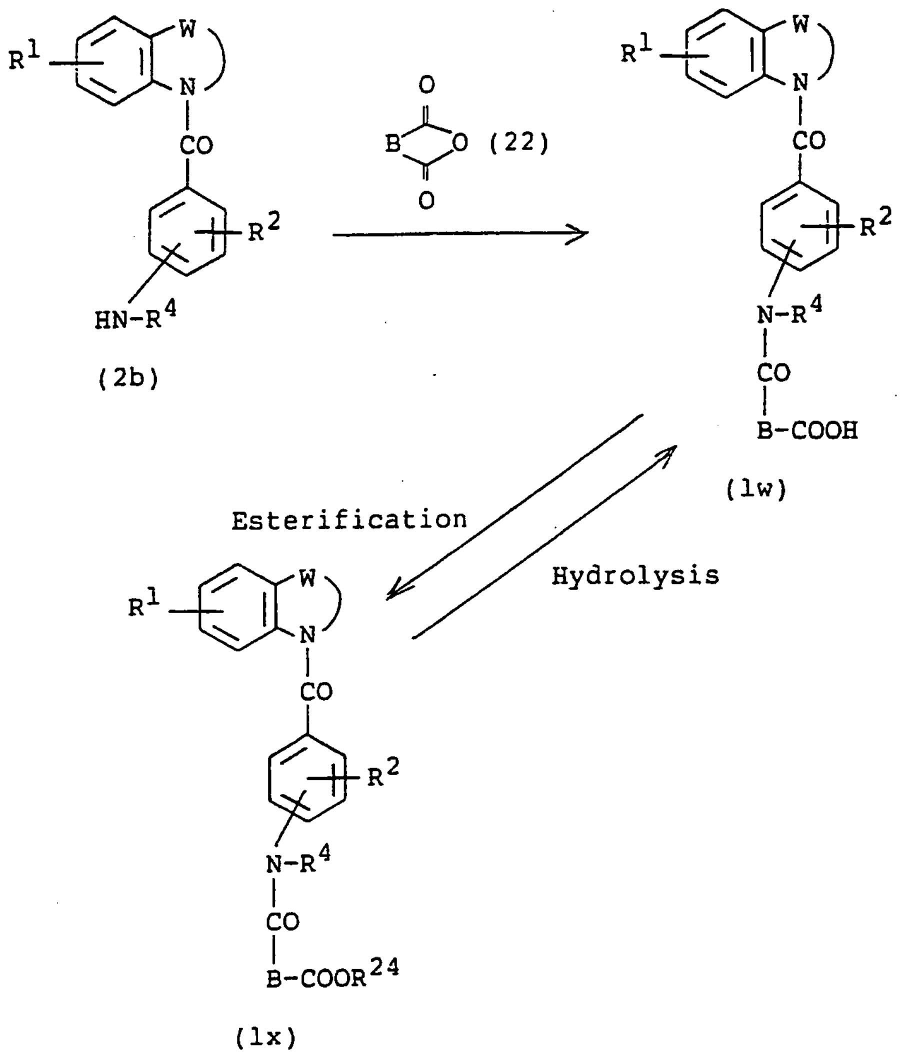


(1u) (1v)

wherein R^1, R^2, R^4, W, R^9, R^{10}, X, and B are as defined above.

The reaction of the compound (1u) and the compound (21) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4. In the reaction, an alkali metal halide (e.g. sodium iodide, potassium iodide, etc.) may be added to the reaction system.

[Reaction Scheme-13]



wherein R^1, R^2, R^4, W, and B are as defined above, and R^{24} is a lower alkyl.

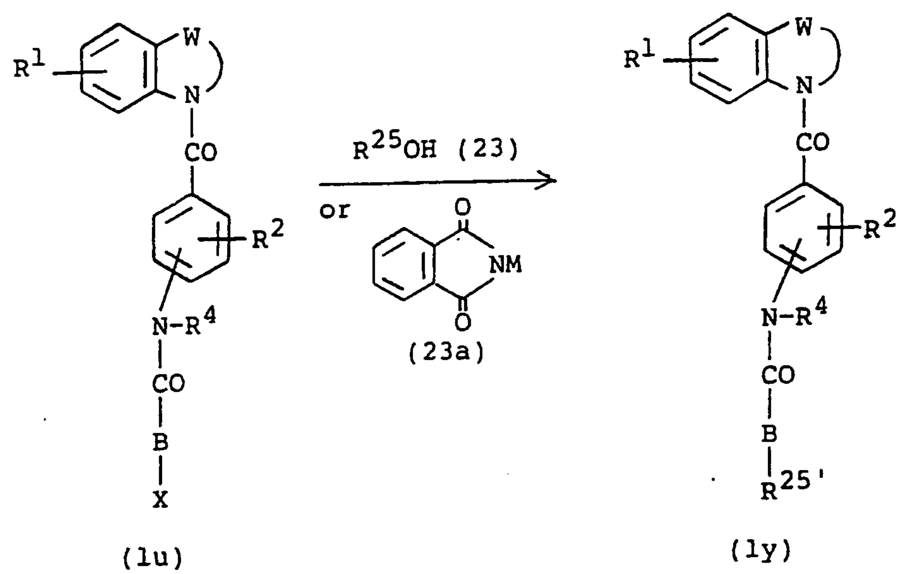
The reaction of the compound (2b) and the compound (22) can be carried out in an appropriate inert solvent. The inert solvent includes, for example, aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), ethers (e.g. tetrahydrofuran, dioxane, diethylene glycol dimethyl

ether, etc.), lower alcohols (e.g. methanol, ethanol, isopropanol, butanol, etc.), halogenated hydrocarbons (e.g. dichloromethane, chloroform, carbon tetrachloride, etc.), acetic acid, ethyl acetate, acetonitrile, dimethylsulfoxide, dimethylformamide, hexamethylphosphoric triamide, and the like. The amount of the compound (2b) and the compound (22) is not critical, but the compound (22) is usually used in an amount of at least one mole, preferably 1 to 2 moles, to 1 mole of the compound (2b). The reaction is usually carried out at a temperature of from about 0°C to about 150°C, preferably from about 0°C to about 100°C, for about 30 minutes to about 10 hours.

The esterification of the compound (1w) is usually carried out by reacting the starting compound with an alcohol (e.g. methanol, ethanol, isopropanol, etc.) in the presence of a mineral acid (e.g. hydrochloric acid, sulfuric acid, etc.) and a halogenating agent (e.g. thionyl chloride, phosphorus oxychloride, phosphorus pentachloride, phosphorus trichloride, etc.) at a temperature of 0°c to 150°C, preferably 50°C to 100°C, for about 1 to 10 hours.

The hydrolysis of the compound (1x) can be carried out under the same conditions as in the hydrolysis of the compound (1j) in the Reaction Scheme-7.

[Reac'ion Scheme-14]



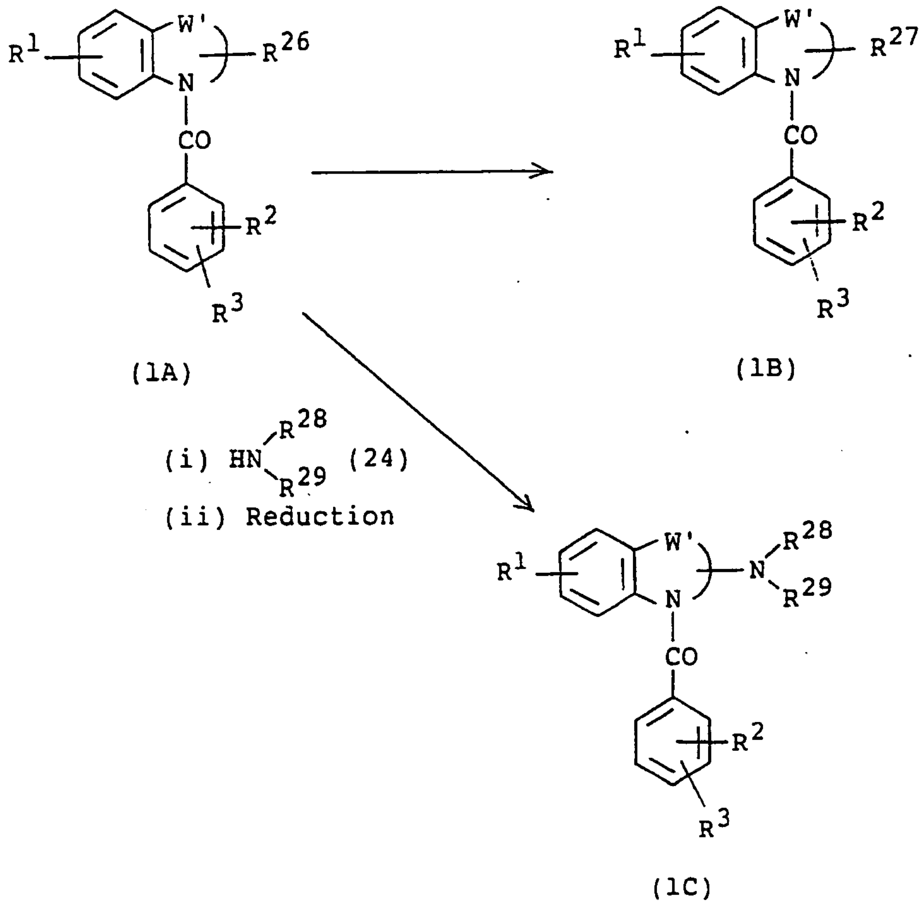
wherein R^1, R^2, R^4, W, B, M, and X are as defined above, and R^{25} is a phenyl which has optionally 1 to 3 substituents selected from a lower alkyl, a lower alkoxy and an amino having optionally a lower alkanoyl substituent, or naphthyl, and $R^{25'}$ is a phenoxy which has optionally 1 to 3 substituents selected from a lower alkyl, a lower alkoxy and an amino having optionally a lower alkanoyl substituent, naphthyloxy or phthalimido.

The reaction of the compound (1u) and the compound (23) or (23a) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

The compound (1y) wherein $R^{25'}$ is phthalimido can be converted into the compound (1y) wherein $R^{25'}$ is amino under the same conditions as in the reaction of converting the compound (1j) into the compound (1k) in the above

Reaction Scheme-7.

[Reaction Scheme-15]



wherein R^1, R^2 and R^3 are as defined above, and R^{26} is oxo, R^{27} is hydroxy, and W' is the same as W, provided that the substituents on the group $-(CH_2)_p-$ or $-CH=CH-(CH_2)_q-$ are 0 to 2, and R^{28} and R^{29} are the same or different and are each hydrogen atom, a lower alkenyl, a cycloalkyl, an oxiranyl-substituted lower alkyl, a lower alkyl having 1 to 2 substituents selected from a lower alkoxy, hydroxy and an amino having optionally a lower alkyl substituent, a phenyl-lower alkyl, a pyridyl-lower alkyl, a cyano-substituted

lower alkyl, a lower alkoxycarbonyl-substituted lower alkyl, a carbamoyl-substituted lower alkyl, a carboxy-substituted lower alkyl, a tetrahydropyranyloxy-substituted lower alkyl, a lower alkanoyloxy-substituted lower alkyl, a piperidinyl which has optionally a phenyl-lower alkyl substituent, an aminocarbonyl-lower alkyl having optionally a lower alkyl substituent, or a lower alkyl, or R^{28} and R^{29} may bind together with the nitrogen atom to which they bond to form a 5- or 6-membered saturated heterocyclic group with or without being intervened with nitrogen or oxygen atom, which heterocyclic ring may optionally have a substituent selected from a lower alkyl, a phenyl-lower alkyl, or a lower alkanoyl.

The conversion of the compound (1A) into the compound (1B) is carried out by reduction thereof. The reducing reaction is preferably carried out by using a hydrogenating reducing agent (e.g. lithium aluminum hydride, sodium boro hydride, diborane, etc.). The reducing agent is usually used in an amount of at least one mole, preferably 1 to 15 moles, to 1 mole of the starting compound. The reducing reaction is usually carried out in an appropriate solvent, for example, water, alcohols (e.g. methanol, ethanol, isopropanol, etc.), ethers (e.g. tetrahydrofuran, diethyl ether, diisopropyl ether, diglyme, etc.), or a mixture of these solvents, at a temperature of from about -60°C to about 150°C, peferably about -30°C to about 100°C, for about 10 minutes to 15 hours. When lithium aluminum

hydride or diborane is used as the reducing agent, it is preferable to use an anhydrous solvent such as tetrahydrofuran, diethyl ether, diisopropyl ether, diglyme, etc.

The reaction of converting the compound (1A) into the compound (1C) is usually carried out in an appropriate solvent or without solvent in the presence or absence of a dehydrating agent. The solvent includes, for example, lower alcohols (e.g. methanol, ethanol, isopropanol, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), halogenated hydrocarbons (e.g. dichloromethane, dichloroethane, chloroform, carbon tetrachloride, etc.), aprotic polar solents (e.g. dimethylformamide, dimethylacetamide, N-methylpyrrolidone, etc.), or a mixture of these solvents. The dehydrating agent includes, for example, conventional drying agent used for dehydrating solvents (e.g. molecular sieves, etc.), mineral acids (e.g. hydrochloric acid, sulfuric acid, borone trifluoride, etc.), organic acids (e.g. p-toluenesulfonic acid, etc.), and the like. The reaction is usually carried out at a temperature of from room temperature to about 250°C, preferably from about 50°C to about 200°C, for about 1 to 48 hours. The amount of the compound (24) is not critical, but it is usually used at least in an equivalent amount, preferably equimolar to largely excess to the amount of the compound (1A). The dehydrating agent is preferably used in a largely excess amount in case of the drying agent and in a catalytic amount in case of the acid.

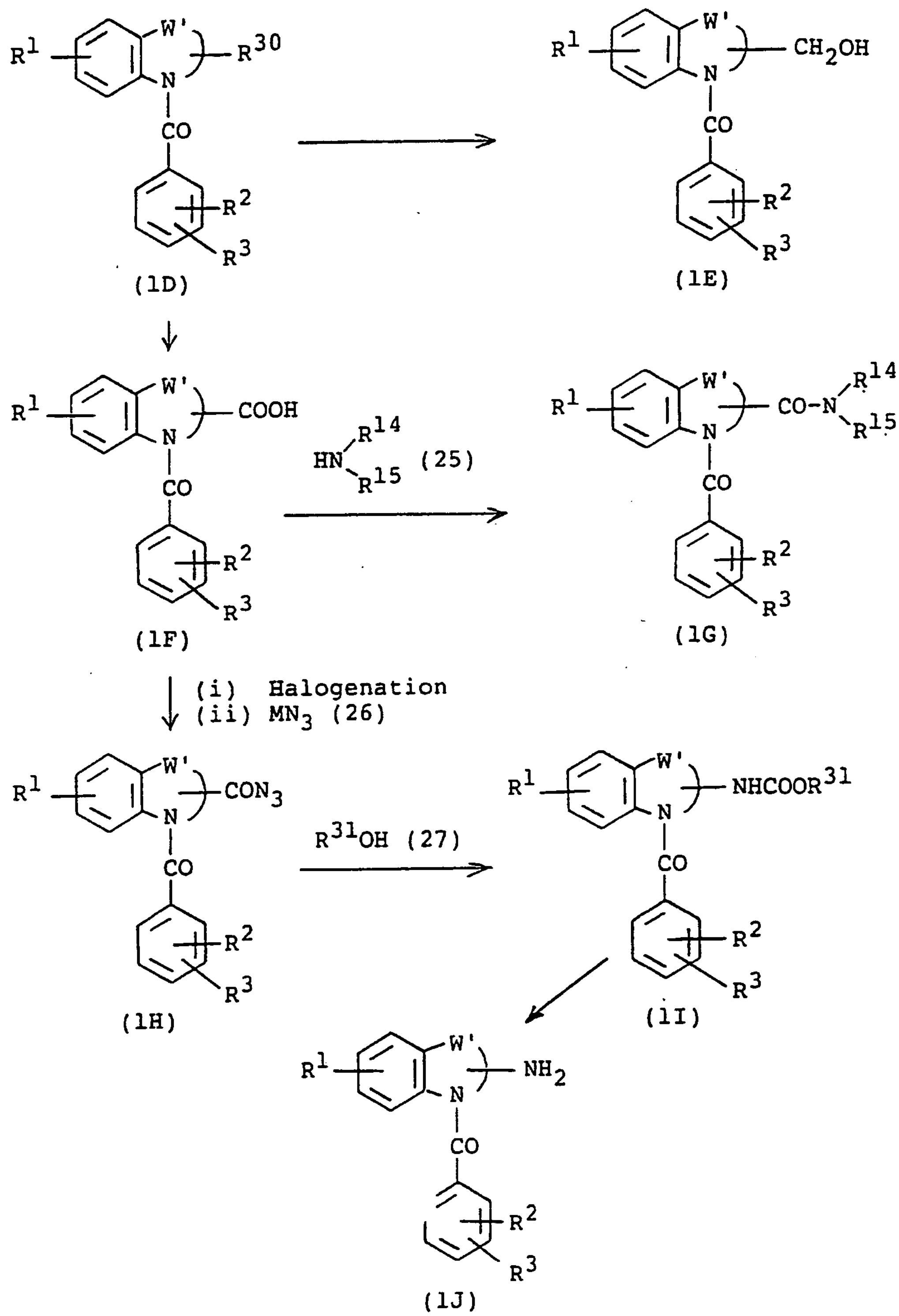
The subsequent reducing reaction can be carried out by various methods, for example by catalytically hydrogenating the compound in an appropriate solvent in the presence of a catalyst. The solvent includes, for example, water, acetic acid, alcohols (e.g. methanol, ethanol, isopropanol, etc.), hydrocarbons (e.g. hexane, cyclohexane, etc.), ethers (e.g. diethylene glycol dimethyl ether, dioxane, tetrahydrofuran, diethyl ether, etc.), esters (e.g. ethyl acetate, methyl acetate, etc.), aprotic polar solvents (e.g. dimethylformamide, etc.), or a mixture of these solvents. The catalyst includes, for example, palladium, palladium black, palladium-carbon, platinum, platinum oxide, copper chromite, Raney nickel, and the like. The catalyst is usually used in an amount of 0.02 to 1 part by weight to 1 part by weight of the starting compound. The reaction is usually carried out at a temperature of from about -20°C to about 100°C, peferably about 0°C to about 70°C, under a hydrogen atmospheric pressure of 1 to 10 atm. for about 0.5 to 20 hours.

Although the reducting reaction can be carried out under the above conditions, it is preferably carried out by using a hydrogenating reducing agent. The hydrogenating reducing agent includes, for example, lithium aluminum hydride, sodium borohydride, diborane, etc., and it is usually used in an amount of at least one mole, preferably 1 to 10 moles, to 1 mole of the compound (1A). The reaction is usually carried out in an appropriate solvent, such as

water, lower alcohols (e.g. methanol, ethanol, isopropanol, etc.), ethers (e.g. tetrahydrofuran, diethyl ether, diglyme, etc.), dimethylformamide, or a mixture of these solvents, at a temperature of about -60°C to about 50°C, preferably about -30°C to room temperature, for about 10 minutes to about 5 hours. When lithium aluminum hydride or diborane is used as the reducing agent, it is preferable to use an anhydrous solvent such as diethyl ether, tetrahydrofuran, diglyme, etc.

The compound (1C) wherein at least one of R^{28} and R^{29} is hydrogen atom can be converted into the compound (1C) wherein at least one of R^{28} and R^{29} is a lower alkyl by reacting the compound (1C) with the compound (8) or the compound (9) under the same conditions as in the reaction of the compound (7) and the compound (8) or (9) in the above Reaction Scheme-4.

[Reaction Scheme-16]



wherein R^1, R^2, R^3, R^{14}, R^{15}, W', and M are as defined above, and R^{31} is a phenyl-lower alkyl, and R^{30} is a lower alkoxycarbonyl.

The reaction of converting the compound (1D) into the compound (1E) can be carried out under the same conditions as in the reaction of converting the compound (1A) into the compound (1B) in the above Reaction Scheme-15.

The reaction of converting the compound (1D) into the compound (1F) can be carried out under the same conditions as in the hydrolysis reaction of the compound (1j) in the above Reaction Scheme-7.

The reaction of the compound (1F) and the compound (25) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The halogenation of the compound (1F) can be carried out under a conventional condition for halogenation of a carboxylic acid. The reaction of the thus-obtained carboxylic acid halide of the compound (1F) with the compound (26) is carried out in an appropriate solvent in the presence or absence of a basic compound. The solvent includes, for example, halogenated hydrocarbons (e.g. methylene chloride, chloroform, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), ethers (e.g. diethyl ether, tetrahydrofuran, dimethoxyethane, etc.), esters (e.g. methyl acetate, ethyl acetate, etc.), aprotic polar solvents

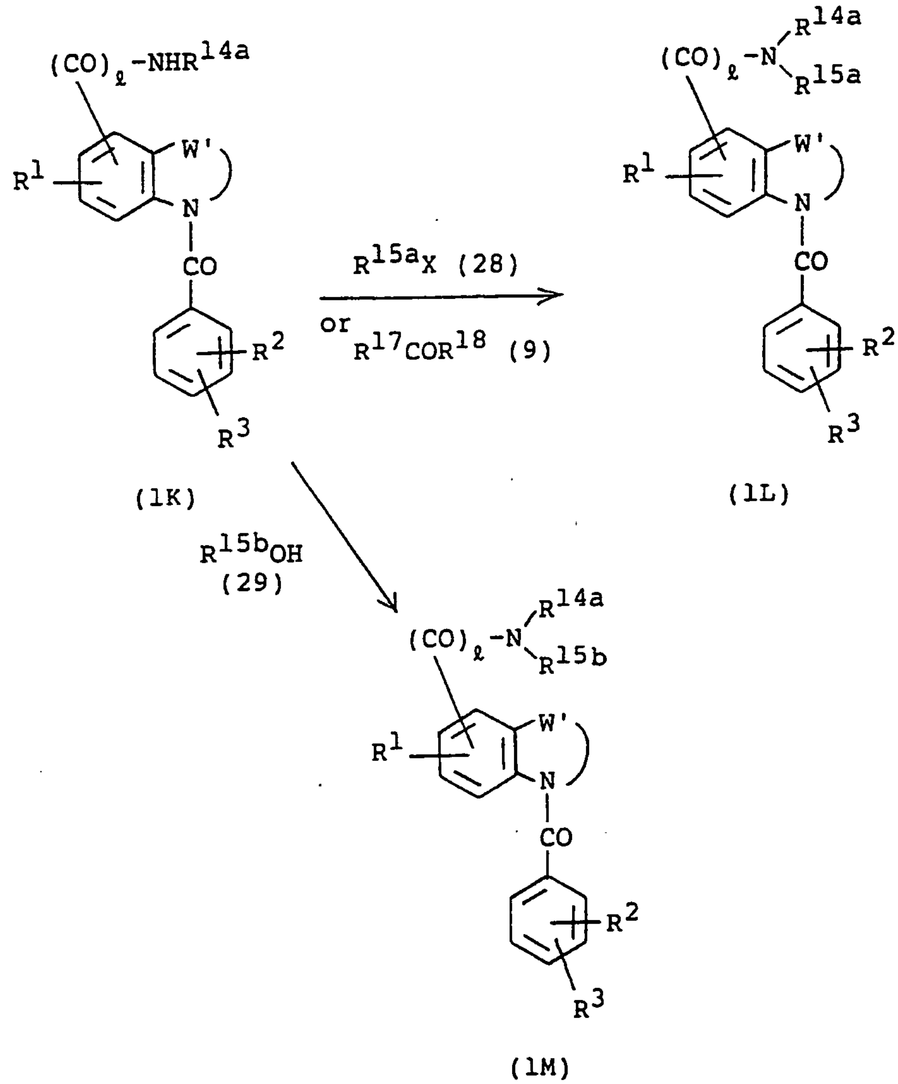
(e.g. N,N-dimethylformamide, dimethylsulfoxide, hexamethylphosphoric triamide, etc.), alcohols (e.g. methanol, ethanol, propanol, butanol, 3-methoxy-1-butanol, ethyl cellosolve, methyl cellosolve, etc.), pyridine, acetone, acetonitrile, water, or a mixture of these solvents. The basic compound includes, for example, organic bases such as triethylamine, trimethylamine, pyridine, dimethylaniline, N-methylmorpholine, DBN, DBU, DABCO, etc., inorganic bases such as potassium carbonate, sodium carbonate, potassium hydroxide, sodium hydroxide, potassium hydride, sodium hydride, silver carbonate, alcoholates (e.g. sodium methylate, sodium ethylate, etc.), and the like. The compound (26) is usually used in an amount of at least 1 mole, preferably 1 to 1.5 mole, to 1 mole of the carboxylic acid halide of the compound (1F). The reaction is usually carried out at a temperature of from -30°C to about 180°C, preferably from about 0°C to about 150°C, for about 5 minutes to 30 hours.

The reaction of the compound (1H) and the compound (27) is carried out in an appropriate solvent or without solvent at a temperature of from about 0°C to about 200°C, preferably from room temperature to about 150°C. The solvent includes the same solvents as used in the above reaction of the carboxylic acid halide of the compound (1F) and the compound (26). The compound (27) is preferably used in an amount largely excess to the the compound (1H). The reaction is usually completed in a reaction time of about 1

to 5 hours.

The reaction of converting the compound (1I) into the compound (1J) can be carried out by reducing the compound. The reducing reaction is usually carried out by catalytically hydrogenating the compound in an appropriate solvent in the presence of a catalyst. The solvent includes, for example, water, acetic acid, alcohols (e.g. methanol, ethanol, isopropanol, etc.), hydrocarbons (e.g. hexane, cyclohexane, etc.), ethers (e.g. dioxane, tetrahydrofuran, diethyl ether, diethylene glycol dimethyl ether, etc.), esters (e.g. ethyl acetate, methyl acetate, etc.), aprotic polar solvents (e.g. N,N-dimethylformamide, etc.), acetic acid, or a mixture of these solvents. The catalyst includes, for example, palladium, palladium black, palladium-carbon, platinum, platinum oxide, copper chromite, Raney nickel, and the like. The catalyst is usually used in an amount of 0.02 to 1 part by weight to 1 part by weight of the starting compound. The reaction is usually carried out at a temperature of from about -20°C to about 100°C, peferably about 0°C to about 80°C, under a hydrogen atmospheric pressure of 1 to 10 atm. for about 0.5 to 20 hours.

[Reaction Scheme-17]



wherein R^1, R^2, R^3, W', ℓ, R^{17}, R^{18}, and X are as defined above, and R^{14a} is hydrogen atom, a lower alkyl, a lower alkanoyl, a lower alkenyl, a cycloalkyl, an oxiranyl-substituted lower alkyl, a lower alkyl having 1 to 2 substituents selected from a lower alkoxy, hydroxy and an amino having optionally a lower alkyl substituent, a phenyl-lower alkyl, a pyridyl-lower alkyl, a lower alkylsulfonyl,

benzoyl, a lower alkoxycarbonyl, anilinocarbonyl, an aminocarbonyl having optionally a lower alkyl substituent, a cyano-substituted lower alkyl, a lower alkoxycarbonyl-substituted lower alkyl, a carbamoyl-substituted lower alkyl, a carboxy-substituted lower alkyl, a tetrahydropyranyloxy-substituted lower alkyl, a lower alkanoyloxy-substituted lower alkyl, a piperidinyl having optionally a phenyl-lower alkyl substituent, a halogen-substituted lower alkanoyl, an imiazolyl-substituted lower alkanoyl, an amino-lower alkanoyl having optionally a substituent selected from a lower alkyl and a lower alkoxycarbonyl, an aminocarbonyl-lower alkyl having optionally a lower alkyl substituent, or a phenyl-lower alkoxycarbonyl, R^{15a} is a lower alkyl, a cycloalkyl, an oxiranyl-substituted lower alkyl, a lower alkyl having 1 to 2 substituents selected from a lower alkoxy, hydroxy and an amino having optionally a lower alkyl substituent, a phenyl-lower alkyl, a pyridyl-lower alkyl, a lower alkylsulfonyl, a cyano-substituted lower alkyl, a lower alkoxycarbonyl-substituted lower alkyl, a carbamoyl-substituted lower alkyl, a carboxy-substituted lower alkyl, a tetrahydropyranyloxy-substituted lower alkyl, a lower alkanoyloxy-substituted lower alkyl, a piperidinyl having optionally a phenyl-lower alkyl substituent, an aminocarbonyl-lower alkyl having optionally a lower alkyl substituent, or a lower alkenyl, and R^{15b} is a lower alkanoyl, a phenyl-lower alkoxycarbonyl, benzoyl, a lower alkoxycarbonyl, a halogen-substituted lower alkanoyl, an

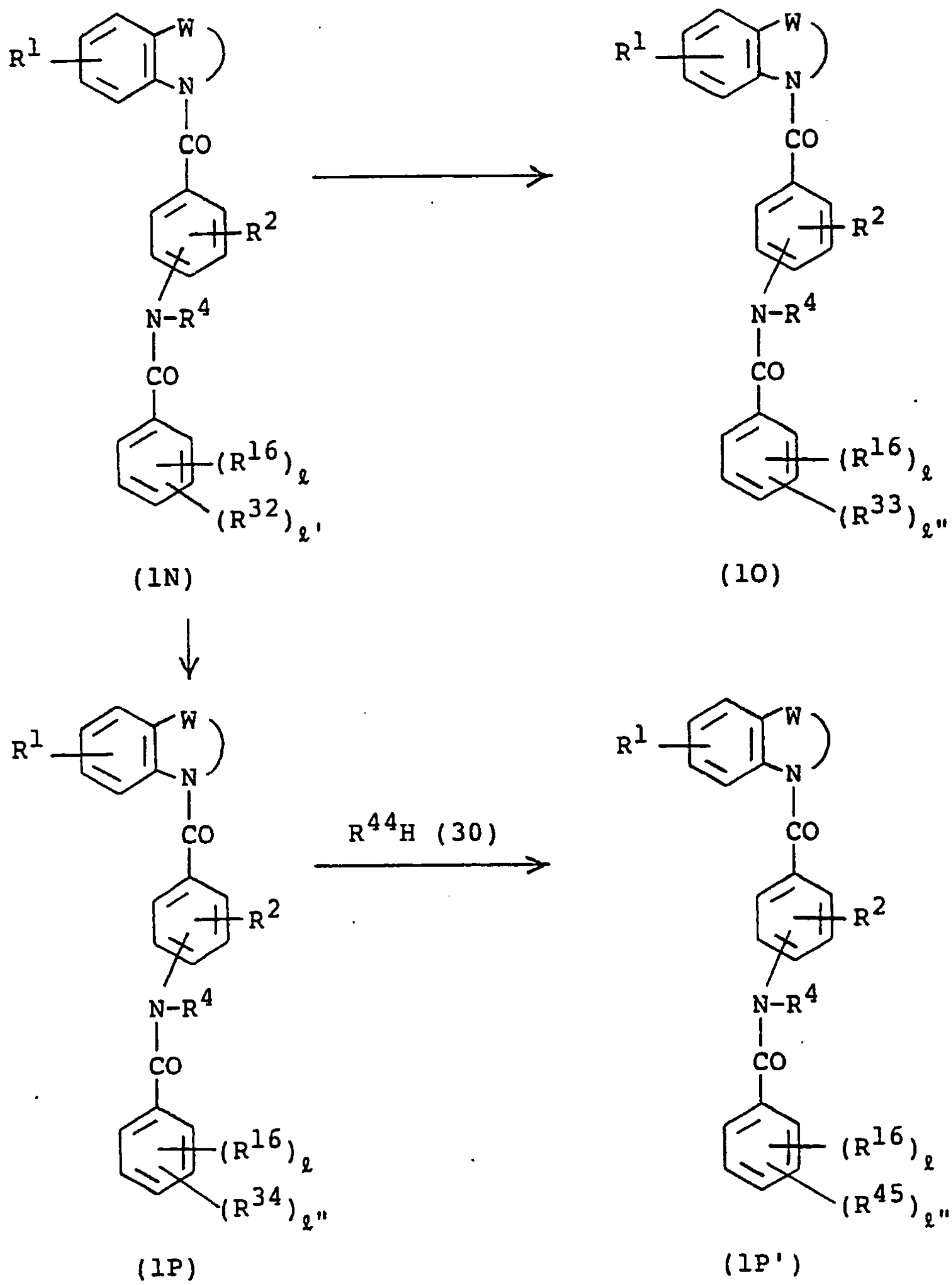
imidazolyl-substituted lower alkanoyl, or an amino-lower alkanoyl having optionally a substituent selected from a lower alkyl and a lower alkoxycarbonyl.

The reaction of the compound (1K) and the compound (28) or the compound (9) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) or the compound (9) in the above Reaction Scheme-4.

The reaction of the compound (1K) and the compound (29) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1. The compound (1M) can also be obtained by reacting the compound (1K) with a compound of the formula $(R^{15b})_2O$ (wherein R^{15b} is as defined above). The reaction can be carried out under the same conditions as in the reaction of the compound (1p) and the compound of the formula: $(R^{7b})_2O$ as described hereinbefore.

The compound (1M) wherein R^{15b} is formyl can also be prepared by reacting the compound (1K) with a formate of the formula: $HCOOR^{82}$ (R^{82} is a lower alkyl). The reaction is usually carried out in the solvent as used in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4 or without solvent, at a temperature of about 0°C to about 200°C, preferably about 0°C to about 170°C, for about 30 minutes to about 30 hours. The formate is preferably used in a largely excess amount to the compound (1K).

[Reaction Scheme-18]



wherein R^1, R^2, R^4, R^{16}, W, ℓ, ℓ'and ℓ" are as defined above, and R^{32} is a lower alkoxycarbonyl-substituted lower alkoxy, R^{33} is a carbamoyl-substituted lower alkoxy, R^{34} is

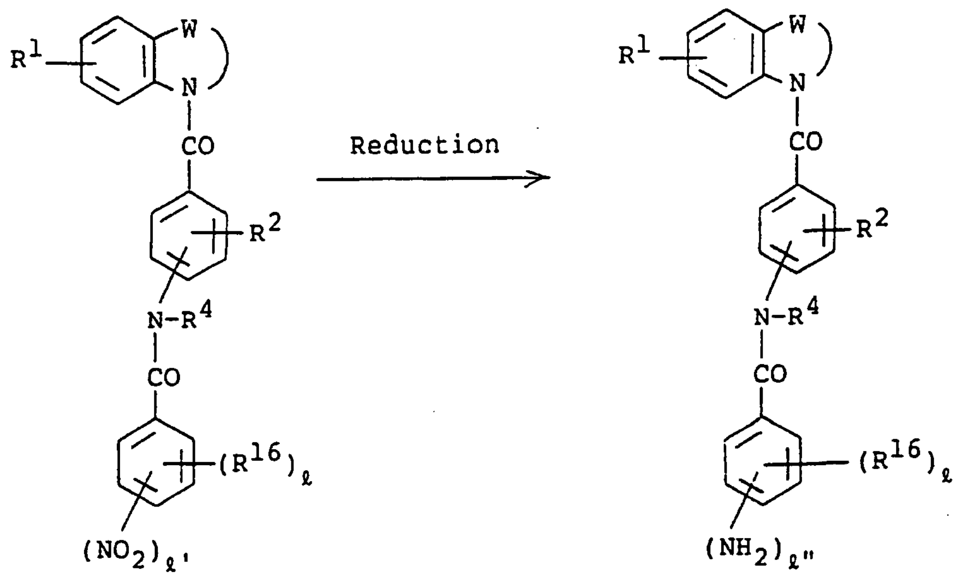
a carboxy-substituted lower alkoxy, R^{44} is an amino having optionally a lower alkyl substituent, and R^{45} is an aminocarbonyl-lower alkoxy having optionally a lower alkyl substituent.

The conversion of the compound (1N) into the compound (1O) can be carried out by reacting the compound with aqueous ammonia in an appropriate solvent in an autoclave. The solvent includes the same solvents as used in the reaction of the carboxylic acid halide and the amine (2) in the above Reaction Scheme-1. The aqueous ammonia is used in a largely excess amount to the compound (1N). The reaction proceeds advantageously by adding an ammonium halide (e.g. ammonium chloride, etc.) to the reaction system. The reaction is usually carried out at a temperature of from room temperature to about 200°C, preferably from room temperature to about 150°C, for about 1 to 10 hours.

The reaction of converting the compound (1N) into the compound (1P) can be carried out under the same conditions as in the hydrolysis of the compound (1j) in the above Reaction Scheme-7.

The reaction of the compound (1P) and the compound (30) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

[Reaction Scheme-19]



(1Q) (1R)

wherein R^1, R^2, R^4, R^{16}, W, ℓ, ℓ' and ℓ'' are as defined above.

The reducing reaction in the above reaction scheme is usually carried out, for example, (i) with a reducing catalyst in an appropriate solvent or (ii) with a reducing agent such as a mixture of a metal or metal salt with an acid, or a mixture of a metal or metal salt with an alkali metal hydroxide, a sulfide or an ammonium salt in an appropriate inert solvent.

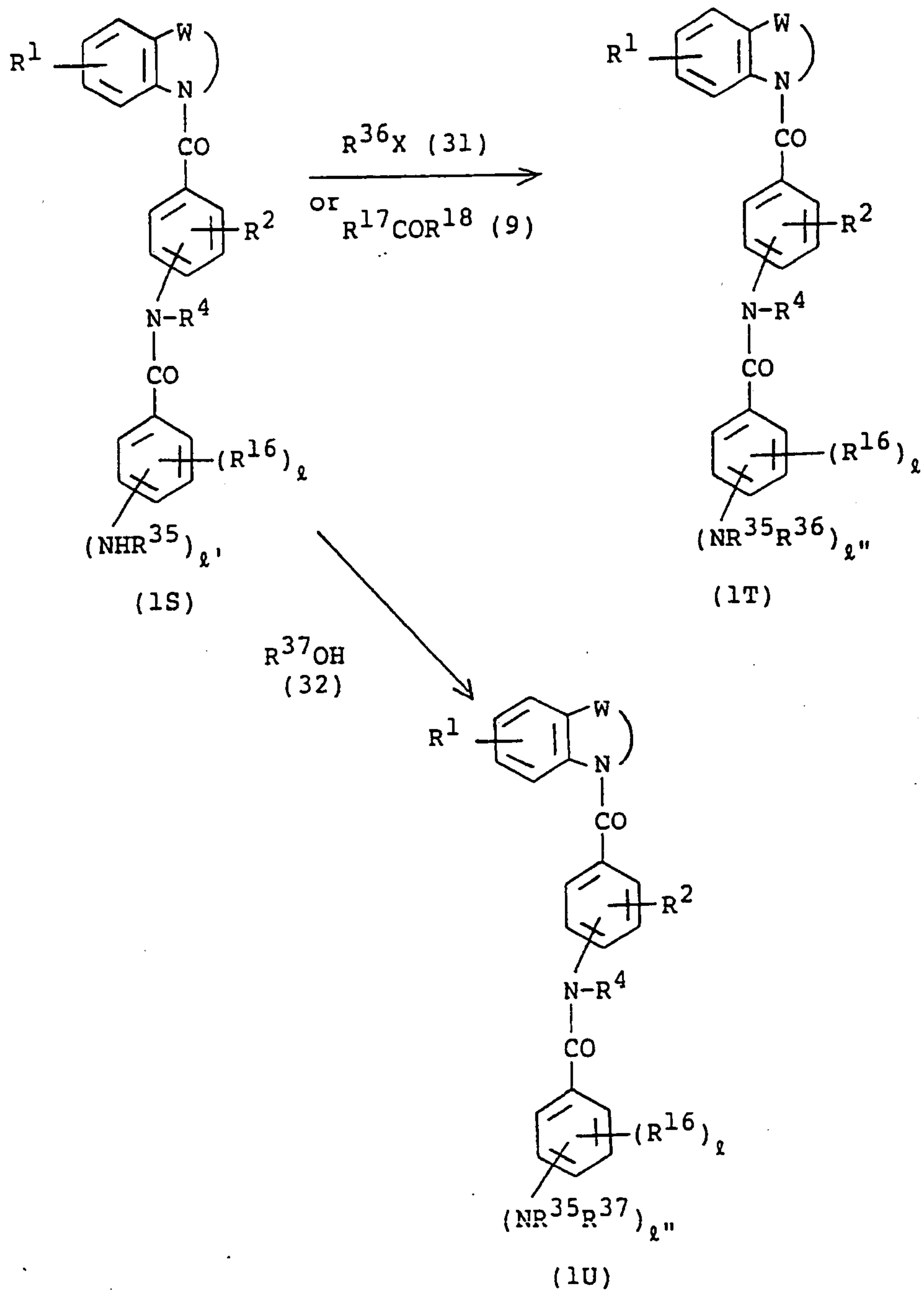
In case of using a reducing catalyst, the solvent includes, for example, water, acetic acid, alcohols (e.g. methanol, ethanol, isopropanol, etc.), hydrocarbons (e.g. hexane, cyclohexane, etc.), ethers (e.g. dioxane, tetrahydrofuran, diethyl ether, diethylene glycol dimethyl ether, etc.), esters (e.g. ethyl acetate, methyl acetate, etc.),

aprotic polar solvents (e.g. N,N-dimethylformamide, etc.), or a mixture of these solvents. The catalyst includes, for example, palladium, palladium black, palladium-carbon, platinum, platinum oxide, copper chromite, Raney nickel, and the like. The catalyst is usually used in an amount of 0.02 to 1 part by weight to 1 part by weight of the starting compound. The reaction is usually carried out at a temperature of from about -20°C to about 150°C, peferably about 0°C to about 100°C, under a hydrogen pressure of 1 to 10 atm. for about 0.5 to 10 hours. In the reaction, an acid such as hydrochloric acid may optionally added to the reaction system.

In case of the above method (ii), the reducting agent includes a mixture of iron, zinc, tin or stannous chloride and a mineral acid (e.g. hydrochloric acid, sulfuric acid, etc.), or a mixture of iron, ferrous sulfate, zinc or tin and an alkali metal hydroxide (e.g. sodium hydroxide, etc.), a sulfide (e.g. ammonium sulfide, etc.), aqueous ammonia, or an ammonium salt (e.g. ammonium chloride, etc.). The inert solvent includes, for example water, acetic acid, methanol, ethanol, dioxane, and the like. The reducing reaction conditions are determined depending on the kinds of the reducting agent, but in case of using a reducing agent comprising stannous chloride and hydrochloric acid, for example, it is preferably carried out at a temperature of about 0°C to room temperature for about 0.5 to 10 hours. The reducing agent is usually used in an

amount of at least one mole, preferably 1 to 5 moles, to 1 mole of the starting compound.

[Reaction Scheme-20]



wherein R^1, R^2, R^4, R^{16}, R^{17}, R^{18}, ℓ, ℓ', ℓ'' and W are as

defined above, and R^{36} is a lower alkyl, R^{37} is a lower alkanoyl, and R^{35} is hydrogen atom, a lower alkyl or a lower alkanoyl.

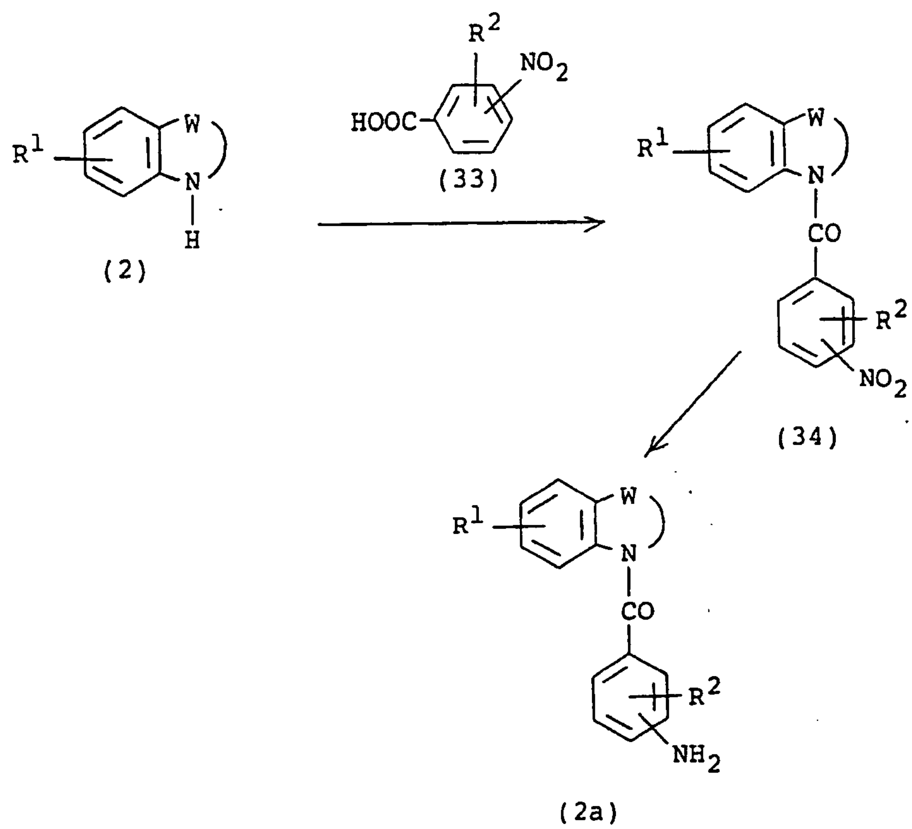
The reaction of the compound (1S) and the compound (31) or the compound (9) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) or the compound (9) in the above Reaction Scheme-4.

The reaction of the compound (1S) and the compound (32) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1. Besides, the compound (1U) can also be obtained by reacting the compound (1S) with a compound of the formula: $(R^{37})_2O$ (R^{37} is as defined above). The reaction is carried out under the same conditions as in the above reaction of the compound (1p) and a compound of the formula: $(R^{7b})_2O$.

The compound (1) wherein R^8 is a phenyl-lower alkoxycarbonyl can be converted into the compound (1) wherein R^8 is hydrogen atom in the same manner as in the reaction of converting the compound (1I) into the compound (1J) in the above Reaction Scheme-16.

Other derivatives of the starting compound (2) can be prepared, for example, by the process shown in the following reaction scheme.

[Reaction Scheme-21]



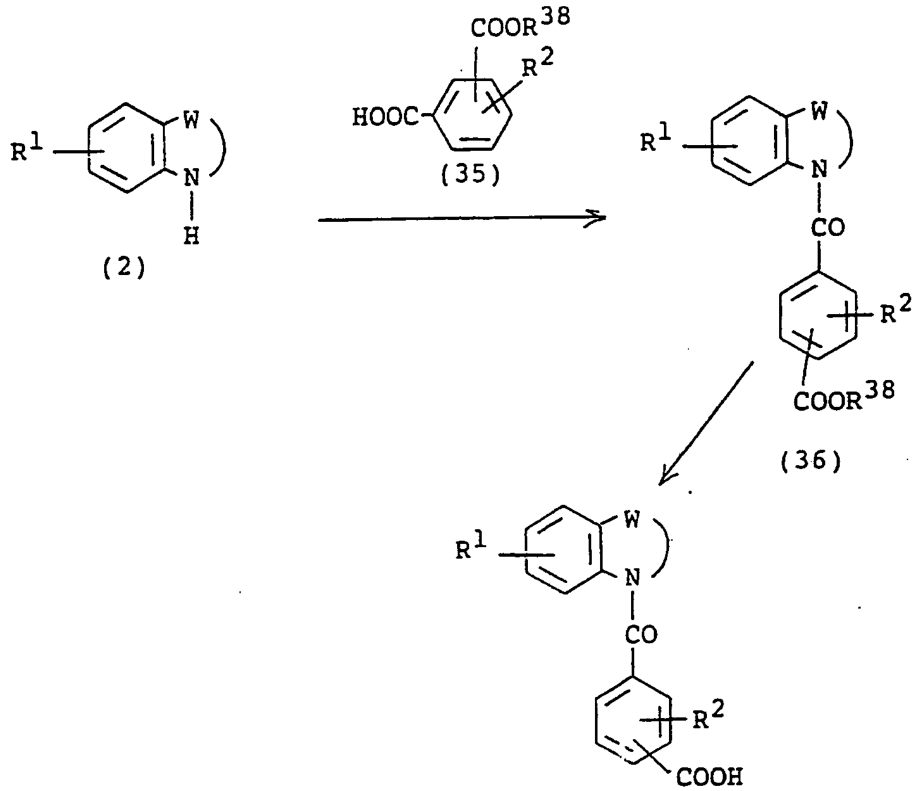
wherein R^1, R^2, and W are as defined above.

The reaction of the compound (2) and the compound (33) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The reaction of converting the compound (34) into the compound (2a) can be carried out under the same conditions as in the reducing reaction in the above Reaction Scheme-19.

The starting compound (5) can be prepared, for example, by the process of the following reaction scheme.

[Reaction Scheme-22]



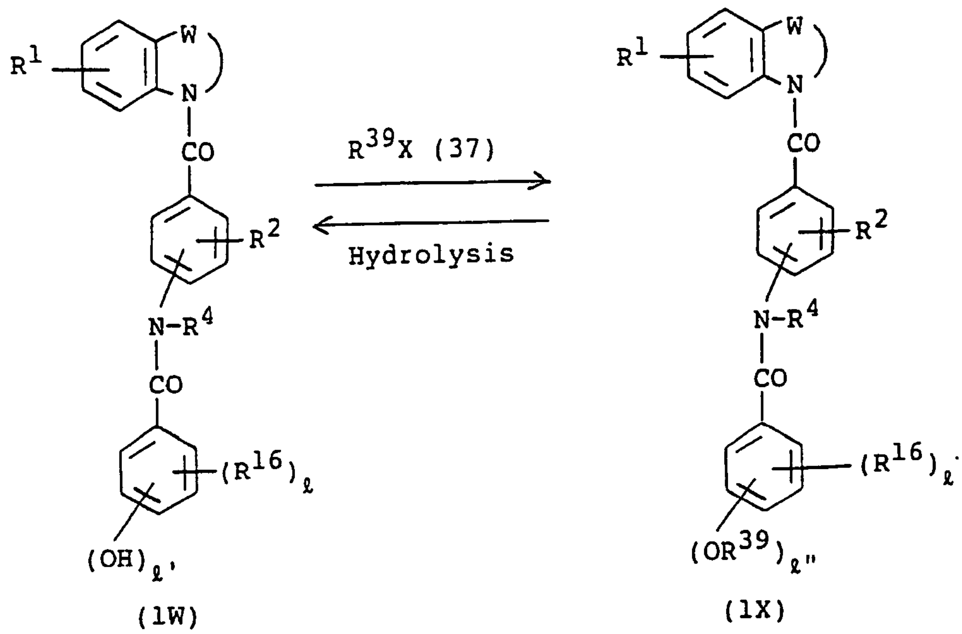
(5)

wherein R^1, R^2, and W are as defined above, and R^{38} is a lower alkyl.

The reaction of the compound (2) and the compound (35) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The reaction of converting the compound (36) into the compound (5) can be carrie out under the same conditions as in the hydrolysi reaction in the above Reaction Scheme-7.

[Reaction Scheme-23]

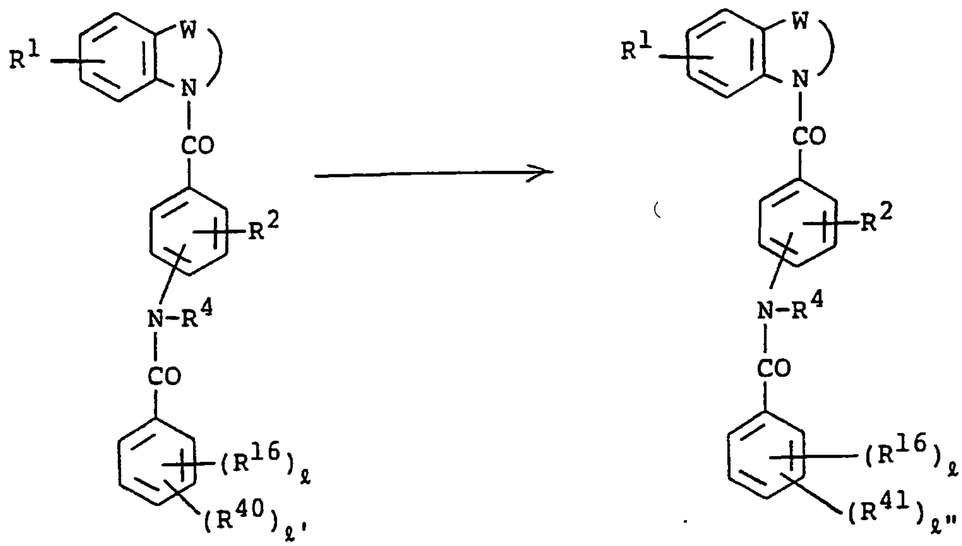


wherein R^1, R^2, R^4, R^{16}, ℓ, ℓ', ℓ'', X, and W are as defined above, and R^{39} is a lower alkanoyl.

The reaction of the compound (1W) and the compound (37) can be carried out under the same conditions as in the reaction of the compound (1n) and the compound (18) in the above Reaction Scheme-9.

The hydrolysis reaction of the compound (1X) can be carried out under the same conditions as in the hydrolysis of the compound (1j) in the above Reaction Scheme-7.

[Reaction Scheme-24]

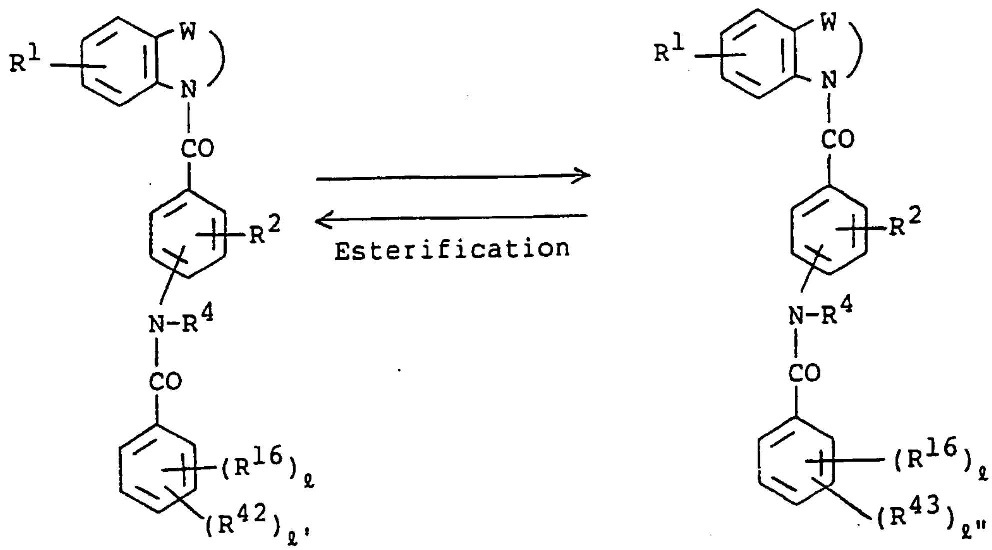


(1Y) (1Z)

wherein R^1, R^2, R^4, R^{16}, ℓ, ℓ', ℓ'', and W are as defined above, R^{40} is a lower alkanoyl, and R^{41} is a hydroxy-substituted lower alkyl.

The reaction of converting the compound (1Y) into the compound (1Z) can be carried out under the same conditions as in the reaction of converting the compound (1A) into the compound (1B) in the above Reaction Scheme-15.

[Reaction Scheme-25]



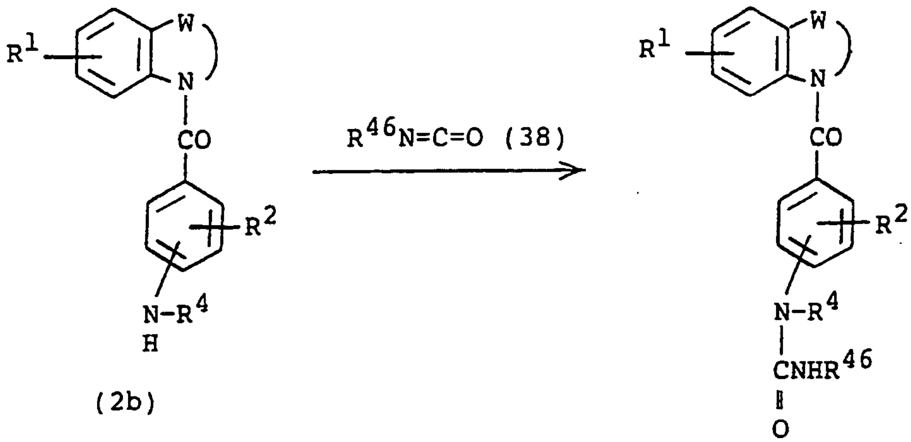
(1aa) (1bb)

wherein R^1, R^2, R^4, R^{16}, ℓ, ℓ', ℓ'', and W are as defined above, R^{42} is a lower alkoxycarbonyl and R^{43} is carboxyl.

The reaction of converting the compound (1aa) into the compound (1bb) can be carried out under the same conditions as in the hydrolysis of the compound (1j) in the above Reaction Scheme-7.

The esterification reaction of the compound (1bb) can be carried out under the same conditions as in the esterification of the compound (1w) in the above Reaction Scheme-13.

[Reaction Scheme-26]



(2b)

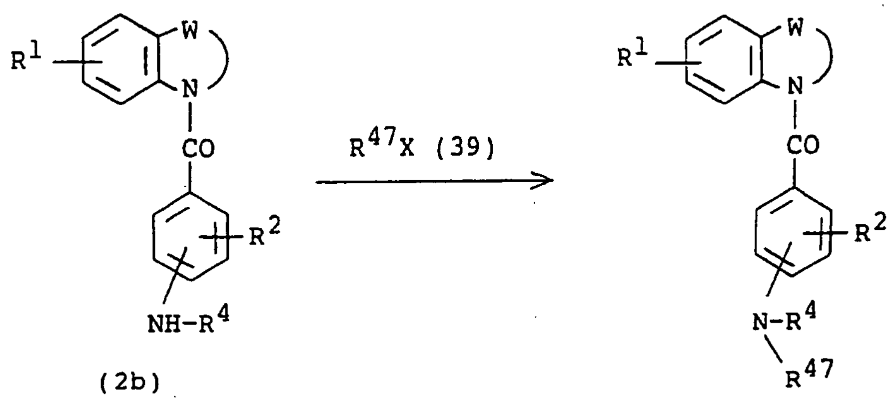
(1cc)

wherein R^1, R^2, R^4, and W are as defined above, and R^{46} is a phenyl having optionally a lower alkyl substituent.

The reaction of the compound (2b) and the compound (38) is usually carried out in an appropriate solvent or without solvent in the presence or absence, preferably in the absence, of a basic compound. The solvent and basic compound are the same as those used in the reaction of the carboxylic acid halide and the amine (2) in the above Reaction Scheme-1.

The compound (38) is usually used in an amount of about 1 to 5 moles, preferably about 1 to 3 moles, to 1 mole of the compound (2b). The reaction is usually carried out at a temperature of from about 0°C to about 200°C, preferably from room temperature to about 150°C, for about 5 minutes to about 30 hours. In the reaction, a boron compound (e.g. boron trifluoride etherate, etc.) may be added to the reaction system.

[Reaction Scheme-27]



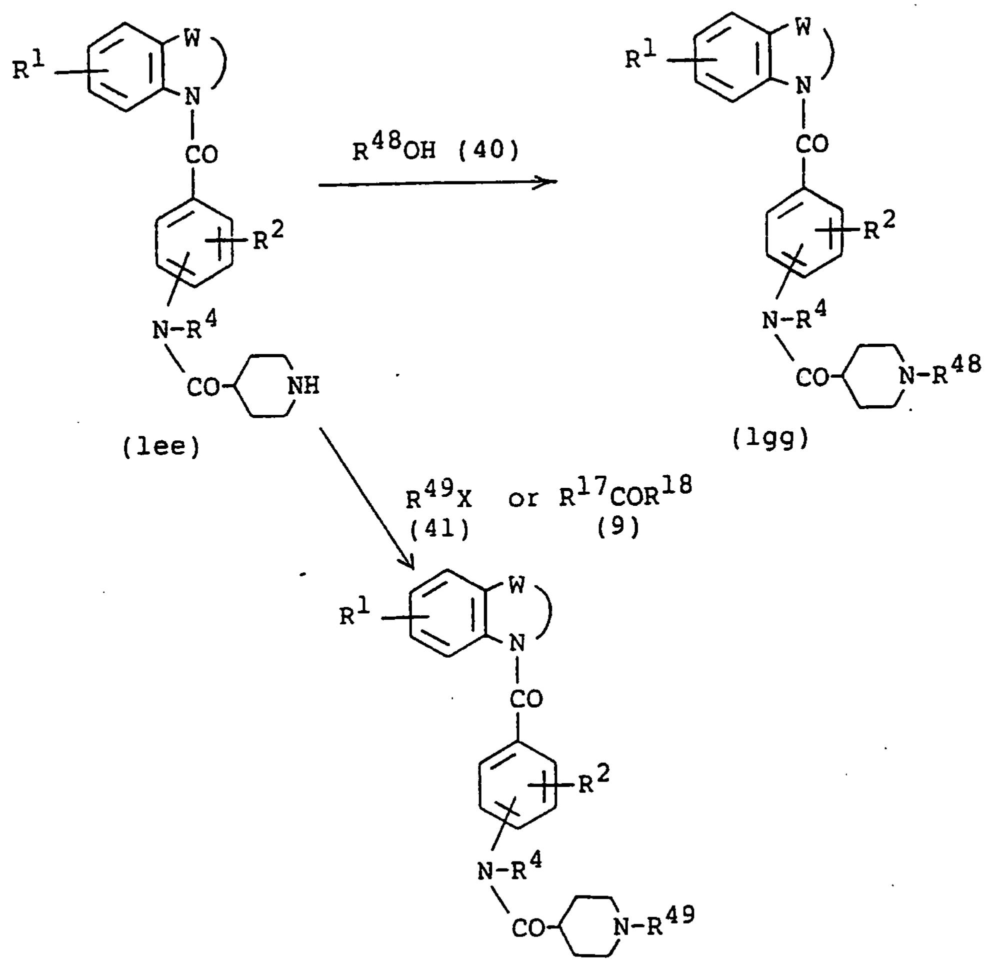
(2b)

(1dd)

wherein R^1, R^2, R^4, W, and X are as defined above, and R^{47} is a phenylsulfonyl which has optionally a substituent selected from a halogen atom and a lower alkyl on the phenyl ring, or quinolylsulfonyl.

The reaction of the compound (2b) and the compound (39) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

[Reaction Scheme-28]



(1ee) (1gg) (1ff)

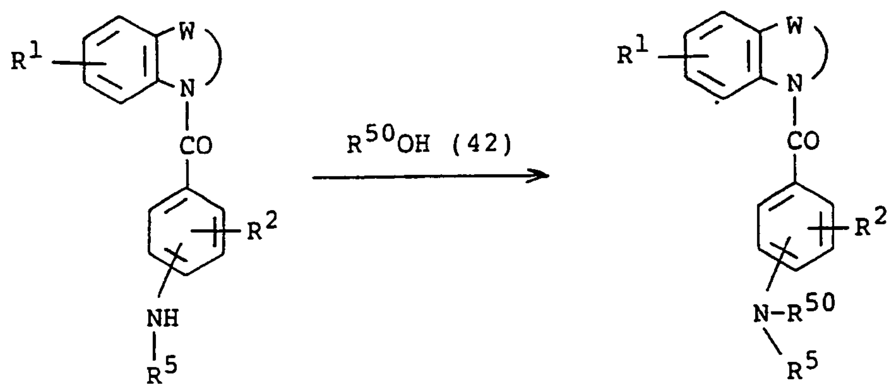
wherein R^1, R^2, R^4, W, R^{17}, R^{18}, and X are as defined above, R^{48} is a phenyl-lower alkoxycarbonyl, a lower alkanoyl, an amino-lower alkanoyl having optionally a lower alkyl substituent, and R^{49} is a lower alkyl or a carbamoyl-lower alkyl.

The reaction of the compound (1ee) and the compound (40) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the

above Reaction Scheme-1.

The reaction of the compound (1ee) and the compound (41) or the compound (9) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) or the compound (9) in the above Reaction Scheme-4, provided that in the reaction product (1ff) produced by the reaction of the compound (1ee) and the compound (9), the group R^{49} is a lower alkyl.

[Reaction Scheme-29]

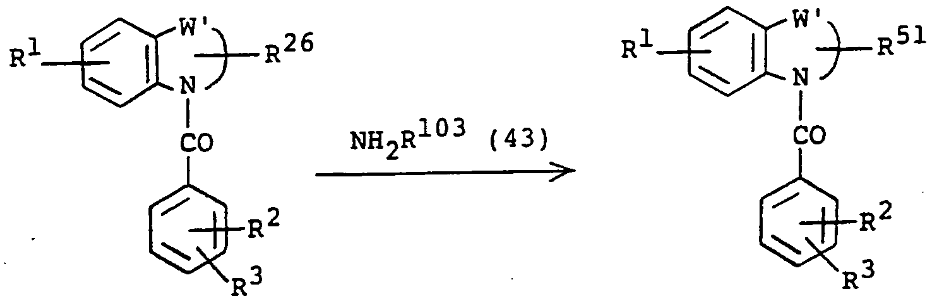


(7) (1hh)

wherein R^1, R^2, R^5, and W are as defined above, and R^{50} is a benzoyl having optionally a halogen substituent on the phenyl ring.

The reaction of the compound (7) and the compound (42) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

[Reaction Scheme-30]



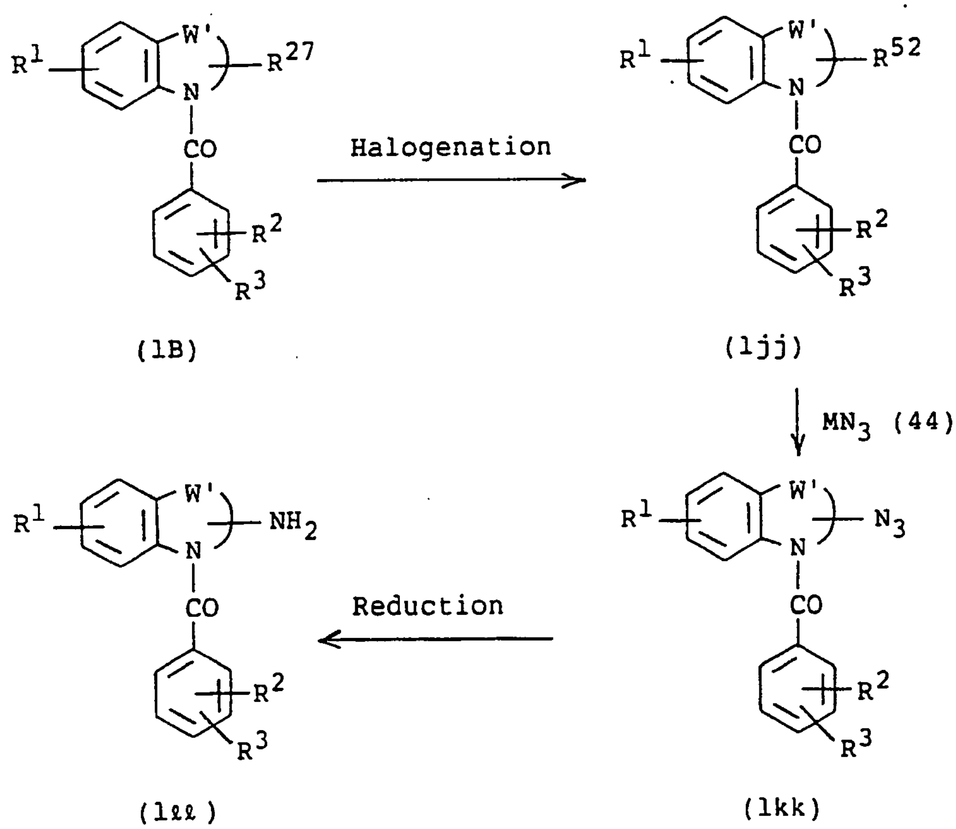
(1A) (1ii)

wherein R^1, W', R^{26}, R^2, and R^3 are as defined above, R^{103} is hydroxy or sulfoxy, and R^{51} is hydroxyimino or sulfoxyimino.

The reaction of the compound (1A) and the compound (43) is usually carried out in an appropriate inert solvent in the presence or absence of a basic compound. The basic compound includes, for example, inorganic basic compounds such as sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, etc., and organic basic compounds such as piperidine, pyridine, triethylamine, 1,5-diazabicyclo[4.3.0]nonene-5 (DBN), 1,8-diazabicyclo-[5.4.0]undecene-7 (DBU), 1,4-diazabicyclo[2.2.2]octane (DABCO), etc. The inert solvent includes, for example, lower alcohols (e.g. methanol, ethanol, isopropanol, etc.), ethers (e.g. dioxane, tetrahydrofuran, diethyl ether, ethylene glycol monomethyl ether, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), halogenated hydrocarbons (e.g. dichloromethane, dichloroethane, chloroform, carbon tetrachloride, etc.), pyridine,

dimethylformamide, dimethylsulfoxide, hexamethylphosphoric triamide, etc., or a mixture of these solvents. The compound (43) is usually used at least in equivalent amount, preferably 1 to 5 moles, to 1 mole of the compound (1A). The reaction is usually carried out at a temperature of from room temperature to about 200°C, preferably from about 50°C to 150°C, for about 1 to 10 hours.

[Reaction Scheme-31]



wherein R^1, W', R^{27}, R^2, M, and R^3 are as defined above, and R^{52} is a halogen atom.

The halogenation of the compound (1B) is usually carried out in an appropriate solvent or without solvent by

reacting the compound (1B) with a halogenating agent.

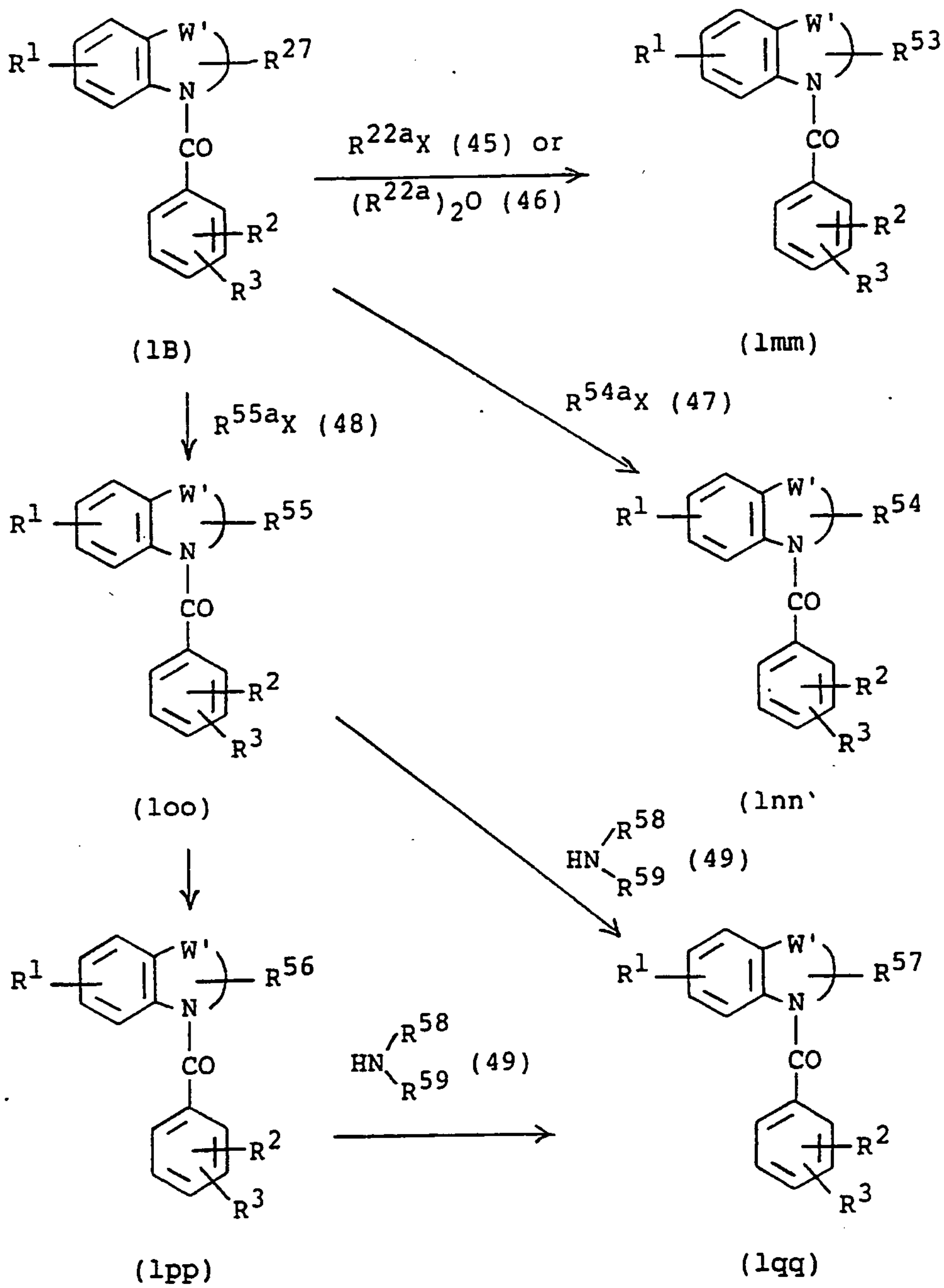
The halogenating agent includes mineral acids (e.g. hydrochloric acid, hydrobromic acid, etc.), N,N-diethyl-1,2,2-trichlorovinylamide, phosphorus pentachloride, phosphorus pentabromide, phosphorus oxychloride, thionyl chloride, methanesulfonyl chloride, or a combination of a phenyl-lower alkyl halide (e.g. p-toluenesulfonyl chloride, etc.) and a basic compound. The basic compound includes the same compounds as used in the reaction of the compound (1A) and the compound (43) in the above Reaction Scheme-30. The solvent includes, for example, ethers (e.g. dioxane, tetrahydrofuran, etc.), halogenated hydrocarbons (e.g. chloroform, methylene chloride, carbon tetrachloride, etc.), and the like. The amount of the halogenating agent may vary depending on the kinds of the halogenating agents, and in case of a combination of a phenyl-lower alkyl halide (e.g. p-toluenesulfonyl chloride, etc.) and a basic compound, it is used in an amount of at least 1 mole, preferably 1 to 2 moles, to 1 mole of the compound (1B), and in case of other halogenating agents, it is used at least in an equimolar amount, usually in a largely excess amount, to the compound (1B). The reaction is usually carried out at a temperature of from room temperature to about 150°C, preferably from room temperature to about 80°C, for about 1 to 80 hours.

The reaction of the compound (1jj) and the compound (44) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the

above Reaction Scheme-4.

The reducing reaction of the compound (1kk) can be carried out under the same conditions as in the reducing reaction using a reducing catalyst for converting the compound (1A) into the compound (1C) in the above Reaction Scheme-15.

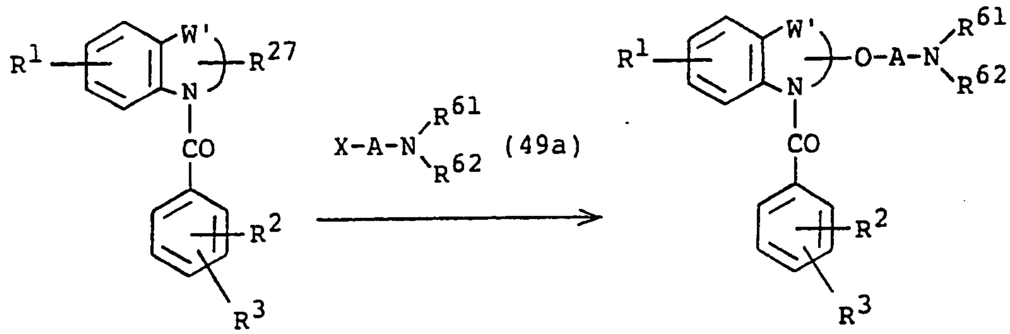
[Reaction Scheme-32A]



wherein R^1, W', R^2, R^3, R^{27}, X, and A are as defined above, R^{53} is a lower alkanoyloxy having optionally a halogen substituent, R^{54} is a lower alkoxy, an amino-lower alkanoyloxy having optionally a lower alkyl substituent, or a group of the formula:

$-O-A-CON\begin{smallmatrix}R^{82}\\R^{83}\end{smallmatrix}$ (A, R^{82} and R^{83} are as defined above), R^{55} is a lower alkoxycarbonyl-substituted lower alkoxy, R^{56} is a carboxy-substituted lower alkoxy, R^{57} is an aminocarbonyl-lower alkoxy having optionally a lower alkyl substituent, R^{54a} is a lower alkyl, an amino-lower alkanoyl having optionally a lower alkyl substituent, or a group of the formula: $-A-CON\begin{smallmatrix}R^{82}\\R^{83}\end{smallmatrix}$ (A, R^{82} and R^{83} are as defined above), R^{55a} is a lower alkoxycarbonyl-substituted lower alkyl, R^{58} and R^{59} are the same or different and are each hydrogen atom or a lower alkyl, and R^{22a} is a lower alkanoyl having optionally a halogen substituent.

[Reaction Scheme-32B]



(1B) (1qq')

wherein R^1, W', R^2, R^3, X, R^{27}, and A are as defined above, and R^{61} and R^{62} are the same or different and are each hydrogen atom, a lower alkyl or a lower alkanoyl.

The reaction of the compound (1B) and the compound (45) or the compound (46) in the Reaction Scheme-32A can be carried out under the same conditions as in the reaction of the compound (1n) and the compound (18) in the above Reaction Scheme-9.

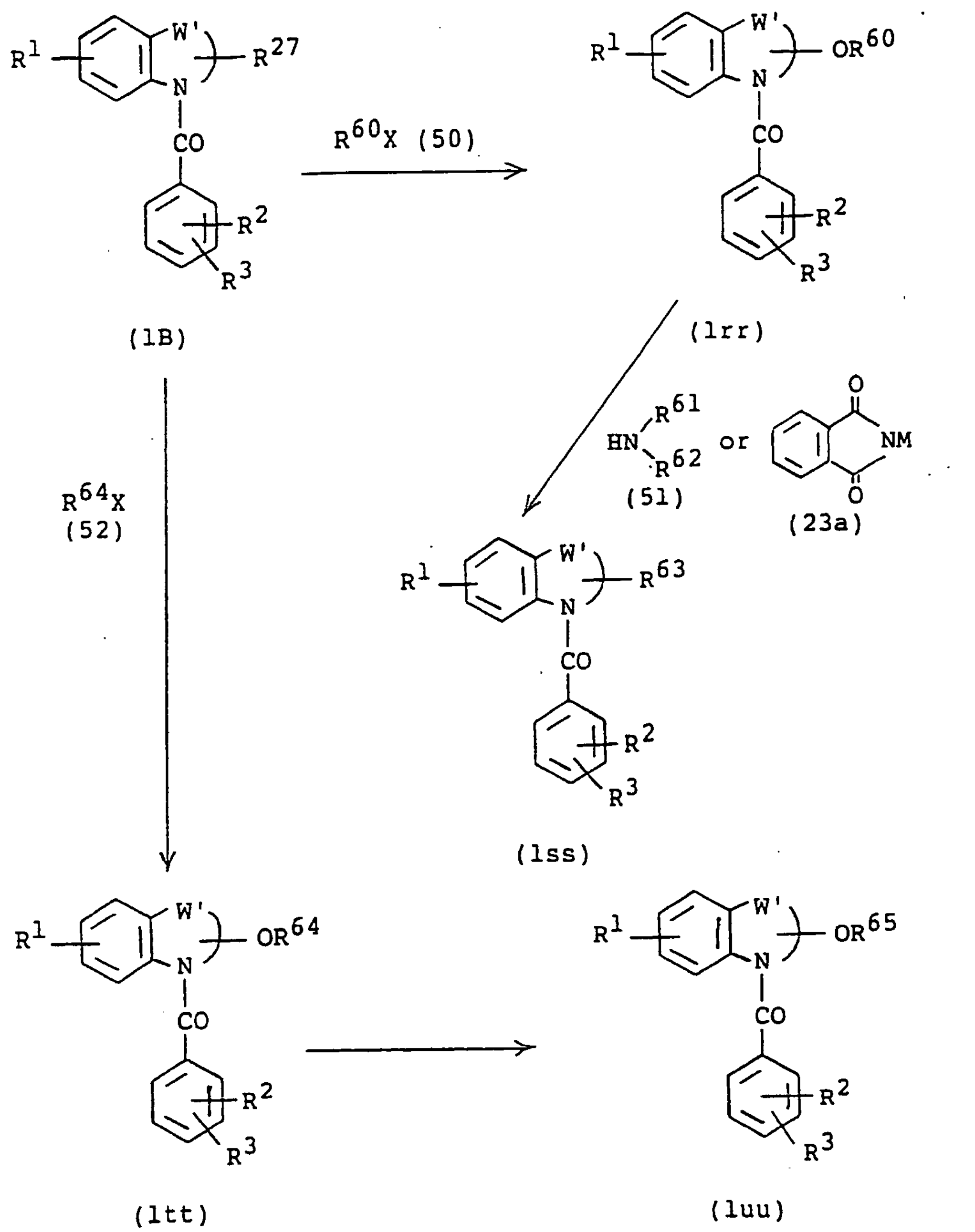
The reaction of the compound (1B) and the compound (47) and the reaction of the compound (1B) and the compound (48) can be carried out under the same conditions as in the reaction of the compound (1n) and the compound (18) in the above Reaction Scheme-9.

The reaction of converting the compound (1oo) into the compound (1pp) can be carried out under the same conditions as in the hydrolysis reaction of the compound (1j) in the above Reaction Scheme-7.

The reaction of the compound (1oo) and the compound (49) and the reaction of the compound (1pp) and the compound (49) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The reaction of the compound (1B) and the compound (49a) in the Reaction Scheme-32B can be carried out under the same conditions as in the reaction of the compound (1n) and the compound (18) in the above Reaction Scheme-9.

[Reaction Scheme-33]



wherein R^1, W', R^2, R^3, R^{27}, R^{61}, R^{62}, M, and X are as defined above, R^{60} is a halogen-substituted lower alkyl, R^{64} is a phthalimido-substituted lower alkyl, R^{63} is an amino-

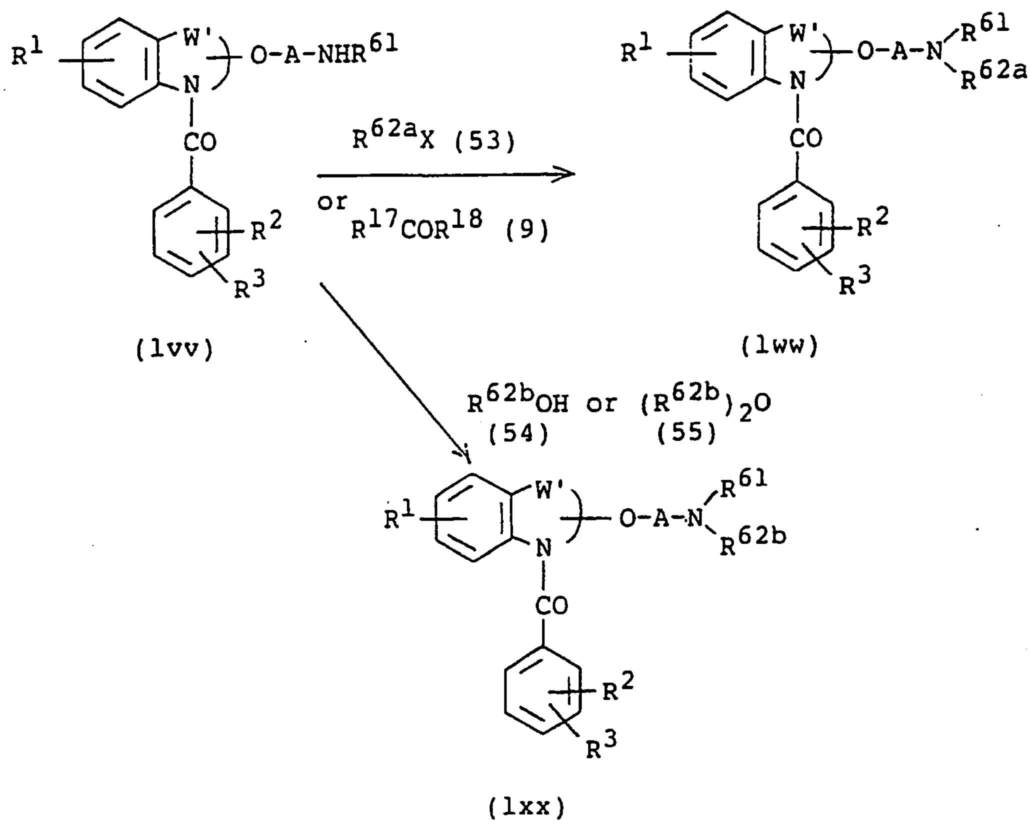
lower alkoxy having optionally a substituent selected from a lower alkyl and a lower alkanoyl, or a phthalimido-substituted lower alkoxy, and R^{65} is an amino-substituted lower alkyl.

The reaction of the compound (1B) and the compound (50) and the reaction of the compound (1B) and the compound (52) can be carried out under the same conditions as in the reaction of the compound (1n) and the compound (18) in the above Reaction Scheme-9.

The reaction of the compound (1rr) and the compound (51) or the compound (23a) can be carried out under the same conditions as in the reaction of the compound (1g) and the compound (14) in the above Reaction Scheme-6.

The reaction of converting the compound (1tt) into the compound (1uu) can be carried out under the same conditions as in the reaction of converting the compound (1j) into the compound (1k) in the above Reaction Scheme-7.

[Reaction Scheme-34]



wherein R^1, R^2, R^3, R^{61}, W', A, R^{17}, R^{18}, and X are as defined above, R^{62a} is a lower alkyl, and R^{62b} is a lower alkanoyl.

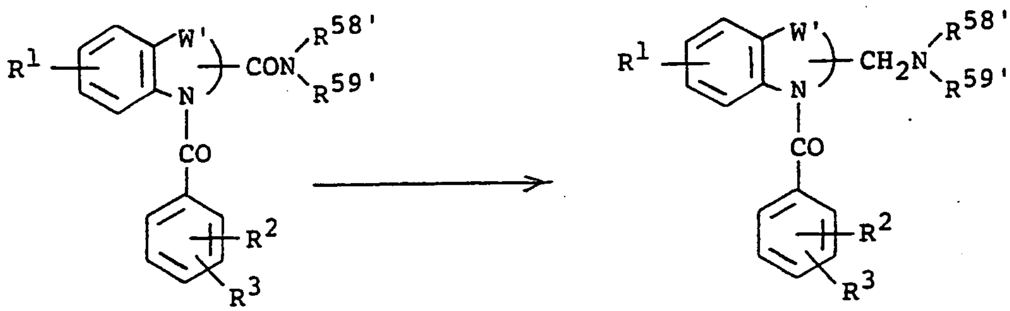
The reaction of the compound (1vv) and the compound (53) or the compound (9) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) or the compound (9) in the above Reaction Scheme-4.

The reaction of the compound (1vv) and the compound (54) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the

above Reaction Scheme-1.

The reaction of the compound (1vv) and the compound (55) can be carried out under the same conditions as in the reaction of the compound (1p) and the compound of the formula: $(R^{7b})_2O$ in the above Reaction Scheme-10.

[Reaction Scheme-35]



(1yy) (1zz)

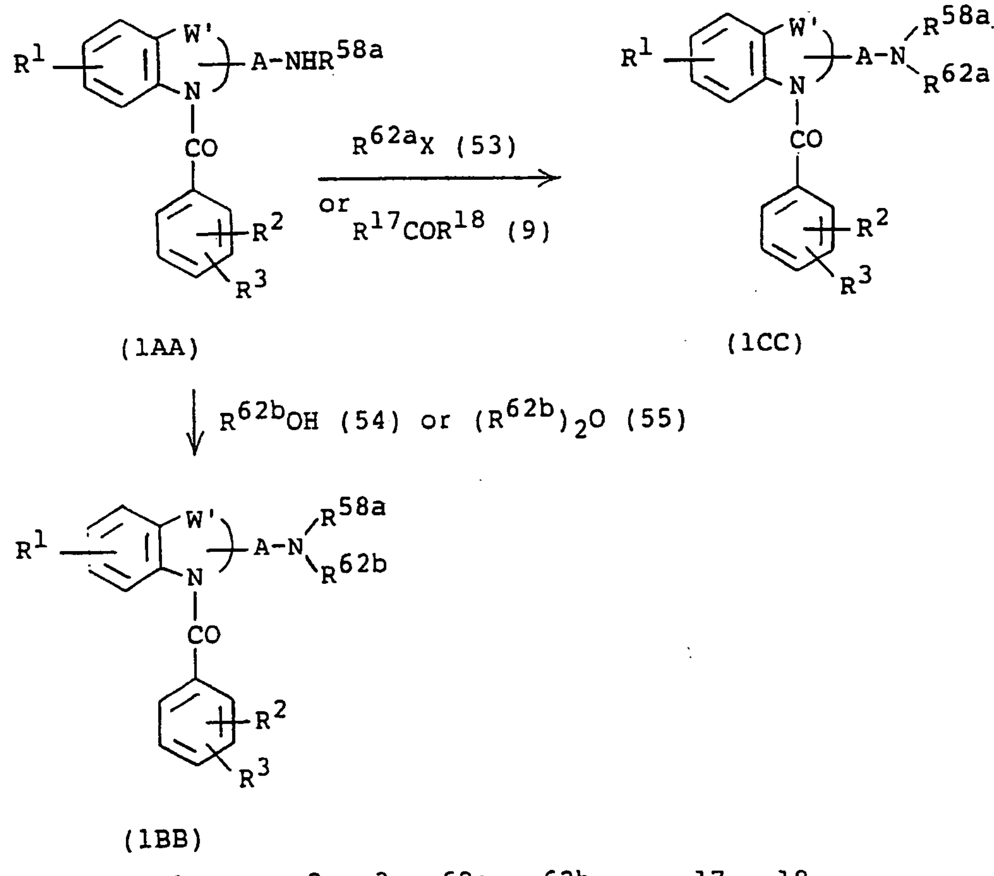
wherein R^1, R^2, R^3, and W' are as defined above, $R^{58'}$ and $R^{59'}$ are the same or different and are each hydrogen atom, a lower alkyl, or a lower alkanoyl.

The reaction of converting the compound (1yy) into the compound (1zz) is usually carried out by reducing the compound (1yy).

The reducing reaction is preferably carried out by using a hydrogenating reducing agent. The hydrogenating reducing agent includes, for example, lithium aluminum hydride, sodium boro hydride, diborane, etc. The reducing agent is usually used in an amount of at least one mole, preferably 1 to 15 moles, to 1 mole of the starting compound. The reducing reaction is usually carried out in an appropriate solvent, such as water, lower alcohols (e.g.

methanol, ethanol, isopropanol, etc.), ethers (e.g. tetrahydrofuran, diethyl ether, diisopropyl ether, diglyme, etc.), or a mixture of these soslvents, at a temperature of about -60°C to about 150°C, preferably about -30°C to 100°C, for about 10 minutes to about 5 hours. When lithium aluminum hydride or diborane is used as the reducing agent, it is preferable to use an anhydrous solvent such as diethyl ether, tetrahydrofuran, diglyme, etc.

[Reaction Scheme-36]



wherein R^1, W', R^2, R^3, R^{62a}, R^{62b}, X, R^{17}, R^{18}, and A are as defined above, R^{58a} is hydrogen atom, a lower alkyl or a lower alkanoyl.

The reaction of the compound (1AA) and the compound (53) or the compound (9) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) or the compound (9) in the above Reaction Scheme-4.

The reaction of the compound (1AA) and the compound (54) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The reaction of the compound (1AA) and the compound (55) can be carried out under the same conditions as in the reaction of the compound (1p) and the compound of the formula: $(R^{7b})_2O$ in the above Reaction Scheme-10.

The compound (1BB) wherein R^{62b} is formyl can also be prepared by reacting the compound (1AA) with a formate of the formula: $HCOOR^{82}$ under the same conditions as in the reaction of the compound (1K) and the compound of the formula: $HCOOR^{82}$ as described hereinbefore.

The compounds of the formula (1) wherein W is sulfur atom or sulfinyl, or R^{82} and R^{83} bind together with the nitrogen atom to which they bond to form thiomorpholino or 1-oxo-thiomorpholino can be converted into the corresponding compounds of the formula (1) wherein W is sulfinyl or sulfonyl, or R^{82} and R^{83} bind together with the nitrogen atom to which they bond to form 1-oxo-thiomorpholino or 1,1-dioxo-thiomorpholino, respectively, by oxidation thereof.

The oxidation reaction is carried out in an

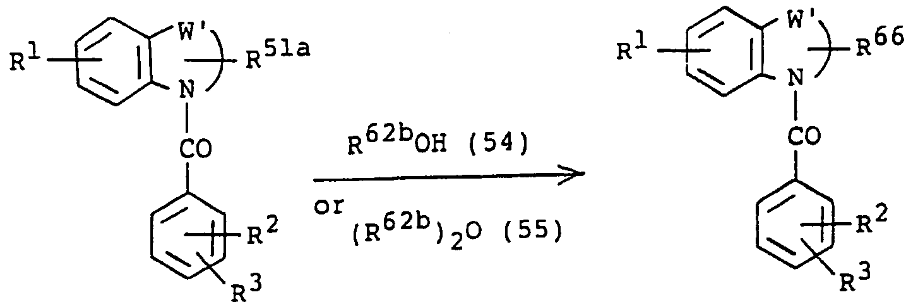
appropriate solvent in the presence of an oxidizing agent. The solvent includes, for example, water, organic acids (e.g. formic acid, acetic acid, trifluoroacetic acid, etc.), alcohols (e.g. methanol, ethanol, etc.), halogenated hydrocarbons (e.g. chloroform, dichloromethane, etc.), or a mixture of these solvents. The oxidizing agent includes, for example, peracids (e.g. performic acid, peracetic acid, trifluoro-peracetic acid, perbenzoic acid, m-chloro-perbenzoic acid, o-carboxy-perbenzoic acid, etc.), hydrogen peroxide, sodium metaperiodate, dichromic acid, dichromates (e.g. sodium dichromate, potassium dichromate, etc.), permanganic acid, permanganates (e.g. potassium permanganate, sodium permanganate, etc.), lead salts (e.g. lead tetraacetate, etc.), and the like. The oxidizing agent is usually used in an amount of at least 1 mole, preferably 1 to 2 moles, to 1 mole of the starting compound. Besides, in cases of the oxidation of converting the sulfur atom into sulfonyl group, the oxidizing agent is usually used at least 2 moles, preferably 2 to 4 moles, to 1 mole of the starting compound. The above reaction is usually carried out at a temperature of about -10°C to about 40°C, preferably from about -10°C to room temperature, for about 1 to 100 hours.

The compound (1) wherein R^{16} or R^2 is a lower alkoxy can be converted into the correspond compound (1) wherein R^{16} or R^2 is hydroxy by heating the compound in a mixture of an acid (e.g. hydrobromic acid, hydrochloric acid, etc.) and a solvent (e.g. water, methanol, ethanol,

isopropyl alcohol, etc.) at 30 to 150°C, preferably at 50 to 120°C.

Besides, the compound (1) wherein R^{16} or R^2 is hydroxy can also be prepared by hydrolysis of the above compound (1) wherein R^{16} or R^2 is a lower alkoxy. The hydrolysis can be carried out in an appropriate solvent in the presence of an acid. The solvent includes, for example, water, lower alcohols (e.g. methanol, ethanol, isopropyl alcohol, etc.), ethers (e.g. dioxane, tetrahydrofuran, etc.), halogenated hydrocarbons (e.g. dichloromethane, chloroform, carbon tetrachloride, etc.), polar solvents (e.g. acetonitrile, etc.), or a mixture of these solvents. The acid includes, for example, mineral acids (e.g. hydrochloric acid, hydrobromic acid, etc.), Lewis acids (e.g. boron trifluoride, aluminum chloride, boron tribromide, etc.), iodides (e.g. sodium iodide, potassium iodide, etc.), or a mixture of the above Lewis acid and iodide. The reaction is usually carried out at a temperature of from room temperature to about 150°C, preferably from room temperature to about 100C, for about 0.5 to 30 hours.

[Reaction Scheme-37]



(1ii')

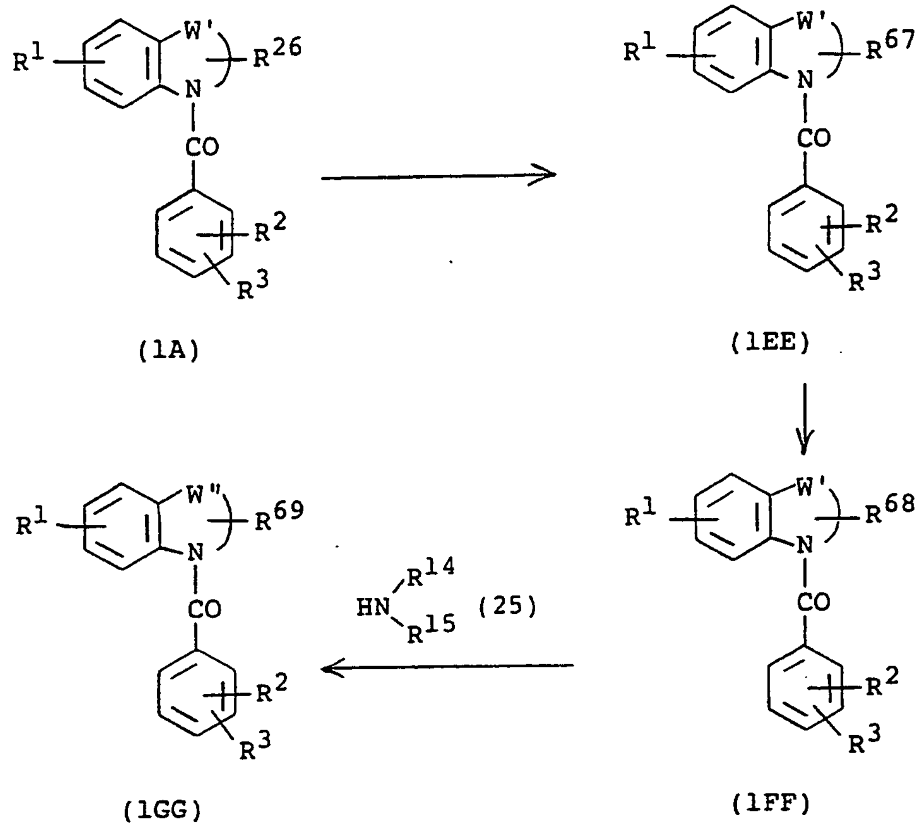
(1DD)

wherein R^1, R^2, R^3, R^{62b}, and W' are as defined above, R^{51a} is hydroxyimino, and R^{66} is a lower alkanoyloxyimino.

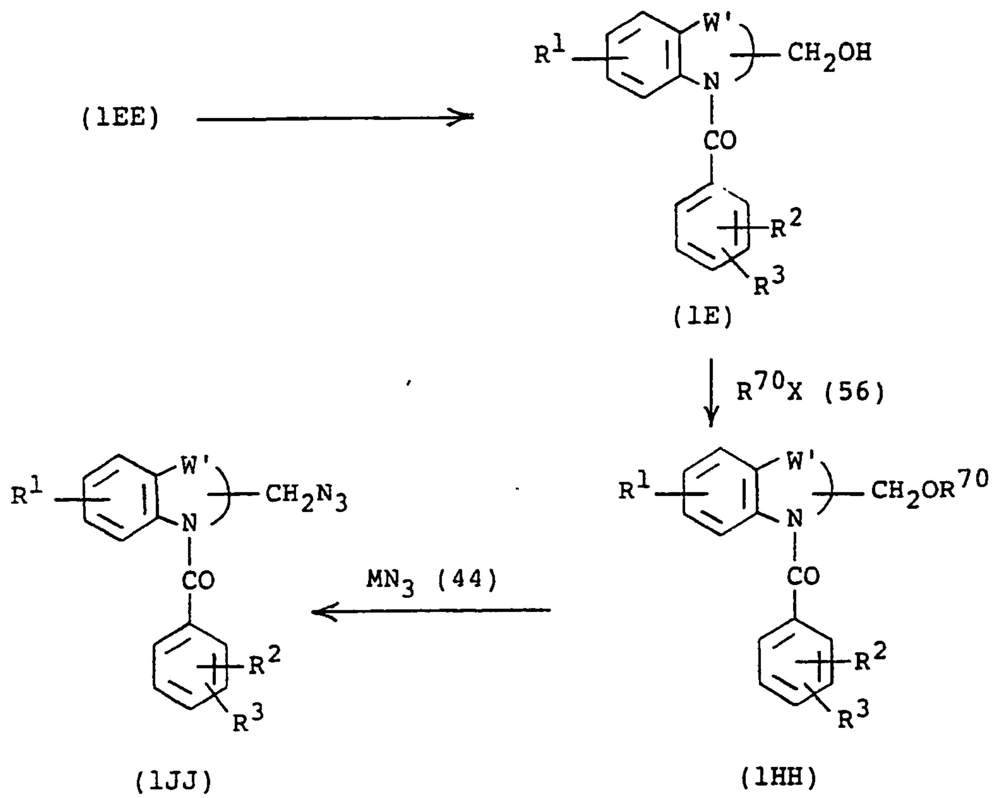
The reaction of the compound (1ii') and the compound (54) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The reaction of the compound (1ii') and the compound (55) can be carried out under the same conditions as in the reaction of the compound (1p) and the compound of the formula: $(R^{7b})_2O$ in the above Reaction Scheme-10.

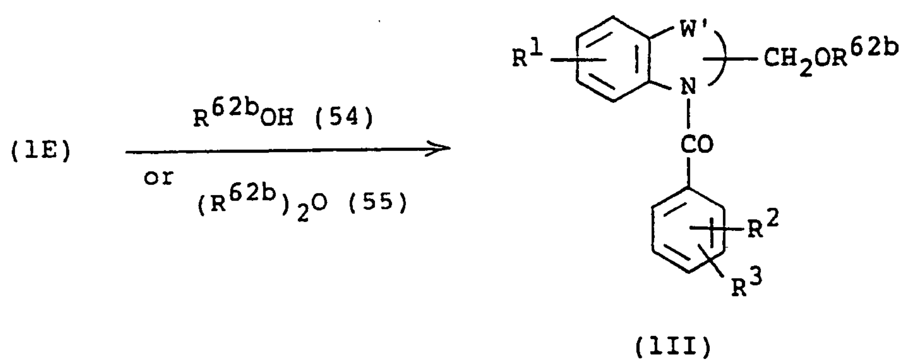
[Reaction Scheme-38A]



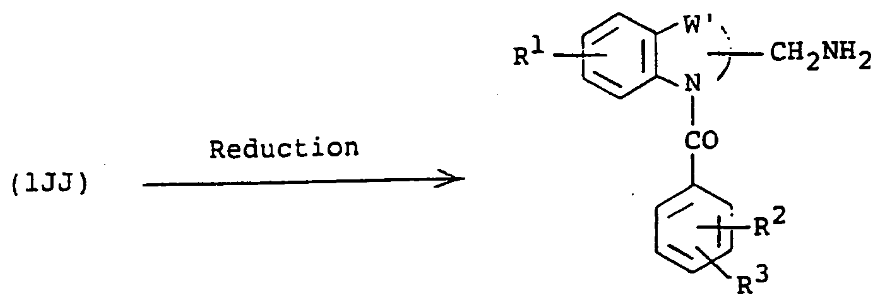
[Reaction Scheme-38B]



[Reaction Scheme-38C]

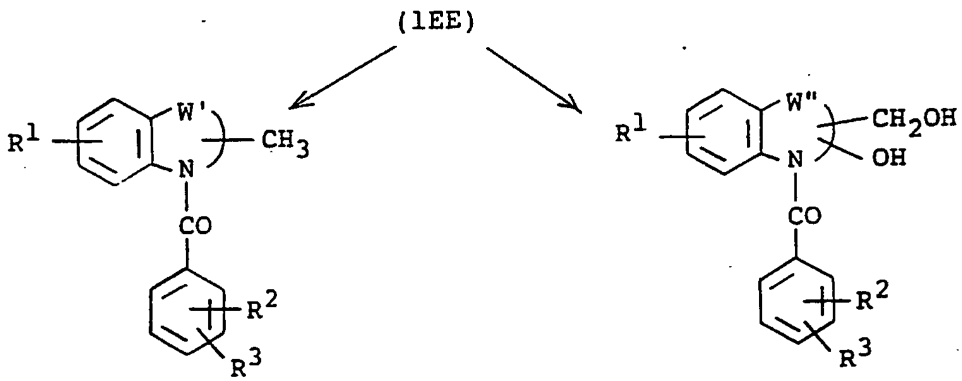


[Reaction Scheme-38D]



(1KK)

[Reaction Scheme-38E]



(1LL) (1MM)

wherein R^1, R^2, R^3, W', R^{26}, R^{14}, R^{15}, R^{62b}, X and M are as defined above, R^{67} is methylidene, R^{68} is a group of the formula: $\diagdown O$, and R^{69} is a group of the formula: $\diagup CH_2OH$ / $\diagdown NR^{14}R^{15}$ (R^{14} and R^{15} are as defined above), or $\diagup CH_2R^{7D}$ / $\diagdown OH$ (R^{7D} is an amino having optionally a substituent selected from a lower alkyl and a lower alkanoyl, R^{70} is a lower alkylsulfonyl, and W" is the same as the above W, provided that the number of the substituent in the groups $-(CH_2)_p-$ and $-CH=CH-(CH_2)_q-$ is 0 or 1.

The reaction of converting the compound (1A) into the compound (1EE) is carried out in an appropriate solvent in the presence of a Wittig reagent and a basic compound. The Wittig reagent includes, for example, a phosphoric compound of the formula:

$$[(R^{71})_3P^+\text{-}CH_2\text{-}R^{72}]X^- \qquad (A)$$

wherein R^{71} is phenyl, R^{72} is hydrogen atom or a lower alkyl, and X is a halogen atom. The basic compound includes inorganic bases (e.g. metallic sodium, metallic potassium, sodium hydride, sodium amide, sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, sodium hydrogen carbonate, etc.), metal alcoholates (e.g. sodium methylate, sodium ethylate, potassium t-butoxide, etc.), alkyl or aryl lithiums or lithium amides (e.g. methyl lithium, n-butyl lithium, phenyl lithium, lithium diisopropylamide, etc.), organic bases (e.g. pyridine, piperidine, quinoline, triethylamine, N,N-dimethylaniline, etc.). The solvent includes any solvent which does not affect on the reaction, for example, ethers (e.g. diethyl ether, dioxane, tetrahydrofuran, monoglyme, diglyme, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), aliphatic hydrocarbons (e.g. n-hexane, heptane, cyclohexane, etc.), amines (e.g. pyridine, N,N-dimethylaniline, etc.), aprotic polar solvents (e.g. N,N-dimethylformamide, dimethylsulfoxide, hexamethylphosphoric triamide, etc.), alcohols (e.g. methanol, ethanol, isopropanol, etc.), and the like. The reaction is usually carried out at a temperature of about -80°C to about 150°C, preferably about -80°C to about 120°C,

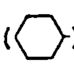
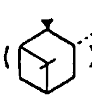
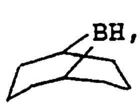
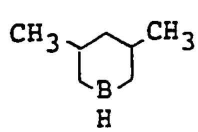
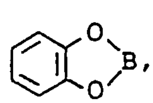
for about 0.5 to 15 hours.

The reaction of converting the compound (1EE) into the compound (1LL) can be carried out under the same conditions as in the catalytically hydrogenation reaction for converting the compound (1A) into the compound (1C) in the above Reaction Scheme-15.

The reaction of converting the compound (1EE) into the compound (1FF) is carried out under the same conditions as in the reaction of converting the compound (1) wherein W is sulfur atom or sulfinyl into the corresponding compound (1) wherein W is sulfinyl or sulfonyl respectively as described herebefore.

The reaction of the compound (1FF) and the compound (25) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

The reaction of converting the compound (1EE) into the compound (1E) can be carried out by firstly subjecting it to hydroboration reaction and then to oxidation.

The hydroboration reaction is carried out in a solvent such as ethers (e.g. diethyl ether, tetrahydrofuran, dioxane, etc.) in the presence of a hydroborating agent at a temperature of from about 0°C to about 50°C, preferaly about 0°C to room temperature, for about 1 to 10 hours. The hydroborating agent includes boron hydride compounds, for example, BH_3.tetrahydrofuran, $BH_3.S(CH_3)_2$, BH_2Cl, $(CH_3)_2CHC(CH_3)_2BH_2$, $(CH_3)_2CHCH(CH_3)BH$, ()$_2$-BH, ()$_2$BH, , , $BHCl_2$, , and the like.

The subsequent oxidation is carried out in water in the presence of an oxidizing agent. The oxidizing agent includes, for example, alkaline hydrogen peroxides (e.g. hydrogen peroxide - sodium hydroxide, etc.), and air oxidation is also used. The reaction is usually carried out at a temperature of from room temperature to about 150°C, preferably from room temperature to about 100°C, for 0.5 to 7 hours.

The hydroborating agent and the oxidizing agent are each used in an amount of at least 1 mole, preferably 1 to 2 mole, to 1 mole of the compound (1EE).

The reaction of the compound (1E) and the compound (54) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The reaction of the compound (1E) and the compound (55) can be carried out under the same conditions as in the reaction of the compound (1p) and the compound of the formula: $(R^{7b})_2O$ in the above Reaction Scheme-10.

The reaction of the compound (1E) and the compound (56) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

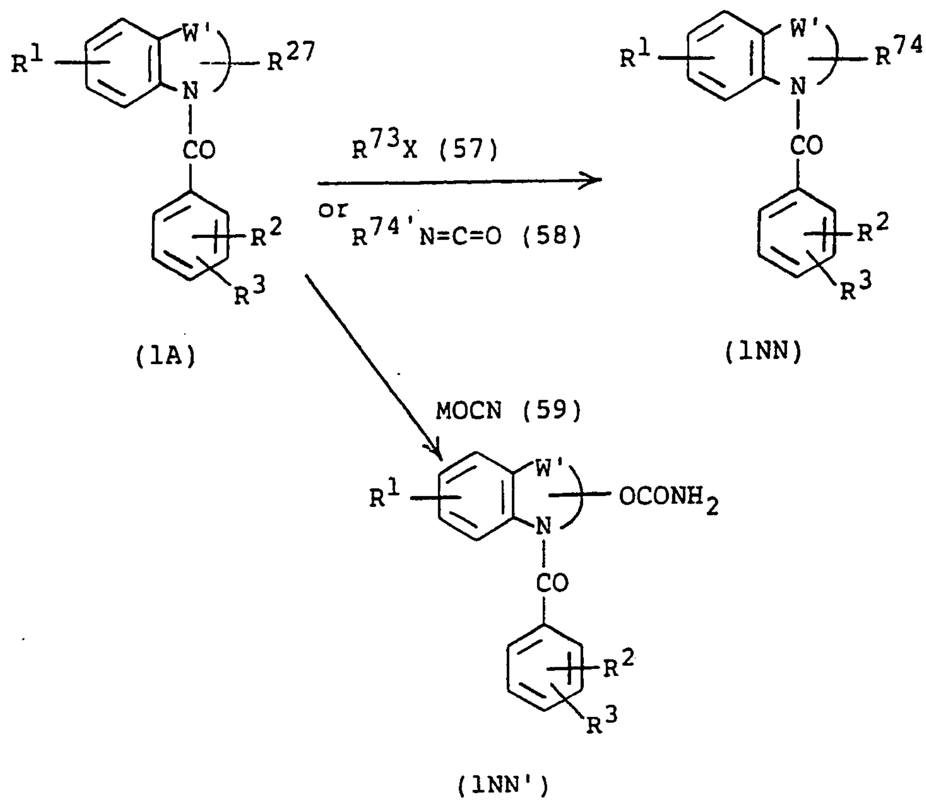
The reaction of the compound (1HH) and the compound (44) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

The reducing reaction of the compound (1JJ) can be carried out under the same conditions as in the catalytic hydrogenation reaction for converting the compound (1A) into the compound (1C) in the above Reaction Scheme-15.

The reaction of converting the compound (1EE) into the compound (1MM) can be carried out by reacting with an oxidizing agent in an appropriate solvent in the presence of a co-oxidizing agent.

The solvent used for the reaction with an oxidizing agent includes, for example, pyridine, ethers (e.g. dioxane, tetrahydrofuran, diethyl ether, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), halogenated hydrocarbons (e.g. dichloromethane, dichloroethane, chloroform, carbon tetrachloride, etc.), esters (e.g. ethyl acetate, etc.), water, alcohols (e.g. methanol, ethanol, isopropanol, t-butanole, etc.), or a mixture of these solvents. The co-oxidizing agent includes, for example, organic amine N-oxides (e g. pyridine N-oxide, N-ethyldiisopropylamine N-oxide, N-methylmorpholine N-oxide, trimethylamine N-oxide, triethylamine N-oxide, etc.). The oxidizing agent includes, for example, osmium tetraoxide, and the like. The oxidizing agent is usually used in an amount of at least 1 mole, preferably 1 to 5 moles, to 1 mole of the starting compound. The reaction is usually carried out at a temperature of from -20°C to 150°C, preferably from room temperature to 100°C, for about 1 to 10 hours.

[Reaction Scheme-39]



wherein R^1, R^2, R^3, R^{27}, W', M, and X are as defined above, R^{73} is an aminocarbonyl having optionally a lower alkyl substituent, R^{74} is an aminocarbonyloxy having optionally a lower alkyl substituent, $R^{74'}$ is a lower alkyl.

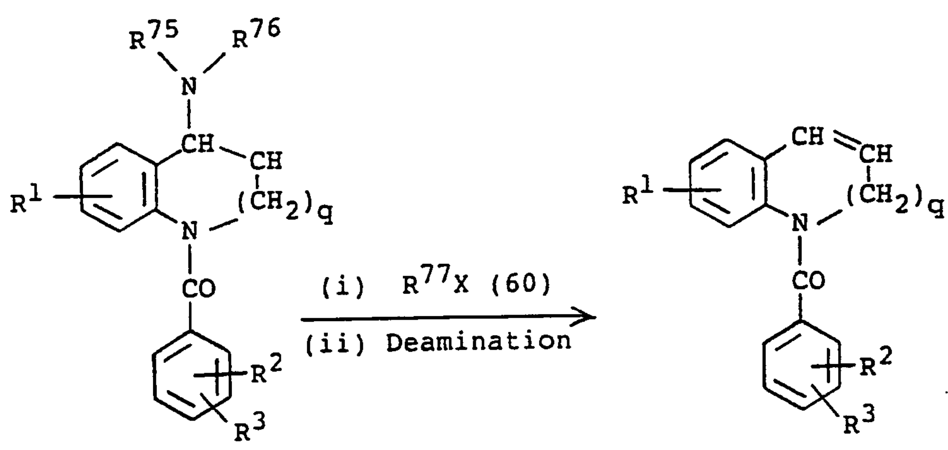
The reaction of the compound (1A) and the compound (57) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

The reaction of the compound (1A) and the compound (59) is carried out in an appropriate solvent in the presence of an acid. The solvent includes the same solvent

as used in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4. The acid includes, for example, mineral acids (e.g. hydrochloride acid, sulfuric acid, etc.), sulfonic acids (e.g. methanesulfonic acid, p-toluenesulfonic acid, etc.), alkanoic acids (e.g. trifluoroacetic acid, etc.), and the like. The compound (59) is used in an amount of at least 1 mole, preferably 1 to 5 moles, to 1 mole of the compound (1A). The reaction is usually carried out at a temperature of from room temperature to about 150°C, preferably from room temperature to about 100°C, for about 1 to 7 hours.

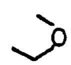
The reaction of the compound (1A) and the compound (58) can be carried out under the same conditions as in the reaction of the compound (2b) and the compound (38) in the above Reaction Scheme-26.

[Reaction Scheme-40]



(100) (1PP)

wherein R^1, R^2, R^3, X, and q are as defined above, and R^{75}, R^{76} and R^{77} are each a lower alkyl, and the carbon atom in the formula: $-(CH_2)_q-$ may be substituted by oxygen atom,

sulfur atom, sulfinyl, sulfonyl, or a group of the formula: $-\overset{R^{13}}{\overset{|}{N}}-$ (R^{13} is as defined above), and further the group: $-(CH_2)_q-$ may optionally have 1 to 3 substituents selected from a lower alkyl having optionally a hydroxy substituent, a lower alkoxy-carbonyl, carboxyl, hydroxy, oxo, a lower alkanoyloxy having optionally a halogen substituent, an amino-lower alkyl having optionally a substituent selected from a lower alkyl and a lower alkanoyl, a lower alkanoyloxy-substituted lower alkyl, a lower alkylsulfonyloxy-lower alkyl, an azido-lower alkyl, a group of the formula: , an aminocarbonyloxy having optionally a lower alkyl substituent, a lower alkoxy, a lower alkoxy-carbonyl-substituted lower alkoxy, a carboxy-substituted lower alkoxy, an aminocarbonyl-lower alkoxy having optionally a lower alkyl substituent, an amino-lower alkoxy having optionally a substituent selected from a lower alkyl and a lower alkanoyl, a phthalimido-substituted lower alkoxy, hydroxyimino, a lower alkanoyloxyimino, a lower alkylidene, a halogen atom, azido, sulfoxyimino, a group of the formula: $R^{81}-\underset{|}{N}-CH_2COO-$ (R^{81} is hydrogen atom or a lower alkyl), hydrazino, pyrrolyl, an amino-lower alkanoyloxy having optionally a lower alkyl substituent, a group of the formula: $-O-A-CO-N\begin{matrix}\diagup R^{82}\\ \diagdown R^{83}\end{matrix}$ (A is as defined above, and R^{82} and R^{83} are the same or different and are each hydrogen atom, a lower alkyl, a carbamoyl-substituted lower alkyl, a hydroxy-substituted lower alkyl, or a pyridyl-lower alkyl, or R^{82} and R^{83} may bind together with nitrogen atom to which they

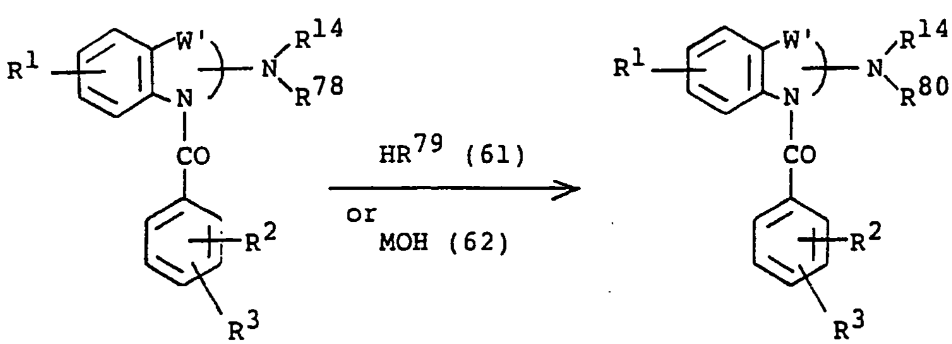
bond to form a 5- or 6-membered saturated heterocyclic group with or without being intervened with nitrogen, oxygen or sulfur atom wherein the heterocyclic group has optionally a substituent selected from oxo, a lower alkyl, a lower alkanoyl, and carbamoyl), and a group of the formula: $-(CO)_n-N\begin{smallmatrix}R^{14}\\R^{15}\end{smallmatrix}$ (n is as defined above, and R^{14} and R^{15} are the same or different and are each hydrogen atom, a lower alkyl, a lower alkenyl, a lower alkanoyl, a cycloalkyl, an oxiranyl-substituted lower alkyl, a lower alkyl having 1 to 2 substituents selected from a lower alkoxy, hydroxy and an amino having optionally a lower alkyl substituent, a phenyl-lower alkyl, a pyridyl-lower alkyl, a lower alkylsulfonyl, benzoyl, a lower alkoxycarbonyl, anilinocarbonyl, an aminocarbonyl having optionally a lower alkyl substituent, a cyano-substituted lower alkyl, a lower alkoxycarbonyl-substituted lower alkyl, a carbamoyl-substituted lower alkyl, a carboxy-substituted lower alkyl, a tetrahydropyranyloxy-substituted lower alkyl, a lower alkanoyloxy-substituted lower alkyl, a piperidinyl having optionally a phenyl-lower alkyl substituent on the piperidinyl ring, a halogen-substituted lower alkanoyl, an imidazolyl-substituted lower alkanoyl, an amino-lower alkanoyl having optionally a substituent selected from a lower alkyl and a lower alkoxycarbonyl, an aminocarbonyl-lower alkyl having optionally a lower alkyl substituent, or a phenyl-lower alkoxycarbonyl, or R^{14} and R^{15} may bind together with the nitrogen atom to which they bond to form a 5- or 6-membered saturated heterocyclic group with or without being intervened with nitrogen or oxygen atom, which

heterocyclic group may optionally have a substituent selected from a lower alkyl, a phenyl-lower alkyl and a lower alkanoyl.

The reaction of the compound (100) and the compound (60) is carried out in an appropriate solvent in an autoclave. The solvent includes any solvent as used in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4. The reaction is usually carried out at a temperature of from room temperature to about 200°C, preferably from room temperature to about 150°C, for about 1 to 7 hours.

The subsequent deamination reaction is carried out in an appropriate solvent in the presence of a basic compound. The solvent includes the same solvent as used in the above reaction of the compound (100) and the compound (60). The basic compound includes any basic compound as used in the reaction of converting the compound (1A) into the compound (1EE) in the above Reaction Scheme-38. The reaction is usually carried out at a temperature of from room temperature to about 150°C, preferably from room temperature to about 100°C, for about 1 to 10 hours.

[Reaction Scheme-41]



(1QQ) (1RR)

wherein R^1, R^2, R^3, R^{14}, M, and W' are as defined above, R^{78} is

an oxiranyl-substituted lower alkyl, R^{79} is a lower alkoxy, or an amino having optionally a lower alkyl substituent, and R^{80} is a lower alkyl having 2 substituents selected from hydroxy, a lower alkoxy, and an amino having optionally a lower alkyl substituent.

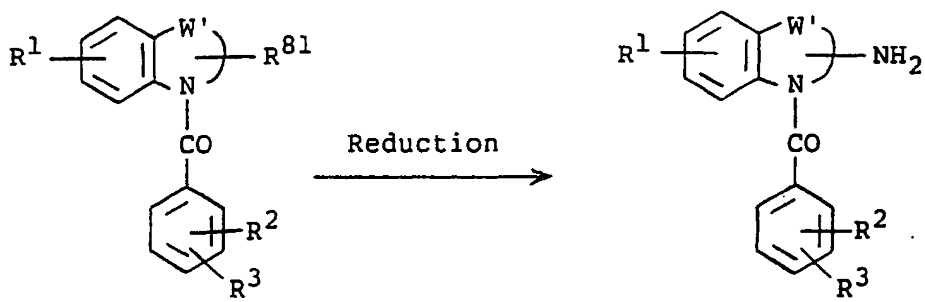
The reaction of the compound (1QQ) and the compound (61) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

The reaction of the compound (1QQ) and the compound (62) can be carried out by firstly reacting them in trifluoroacetic acid at a temperature of about 0°C to about 100°C, preferably about 0°C to about 50°C, for about 1 to 7 hours, followed by hydrolysis of the resultant.

The hydrolysis is carried out in an appropriate solvent or without solvent in the presence of an acid or a basic compound. The solvent includes, for example, water, lower alcohols (e.g. methanol, ethanol, isopropanol, etc.), ketones (e.g. acetone, methyl ethyl ketone, etc.), ethers (e.g. dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, etc.), fatty acids (e.g. acetic acid, formic acid, etc.), or a mixture of these solvents. The acid includes, for example, mineral acids (e.g. hydrochloric acid, sulfuric acid, hydrobromic acid, etc.), organic acids (e.g. formic acid, acetic acid, aromatic sulfonic acid, etc.), and the like. The basic compound includes, for example, metal carbonates (e.g. sodium carbonate, potassium carbonat , etc.), metal hydroxides (e.g. sodium hydroxide, potassium hydroxide, calcium hydroxide,

etc.). The reaction is usually carried out at a temperature of from room temperature to about 200°C, preferably from room temperature to about 150°C, for about 0.5 to 25 hours.

[Reaction Scheme-42]



(1SS) (1ℓℓ)

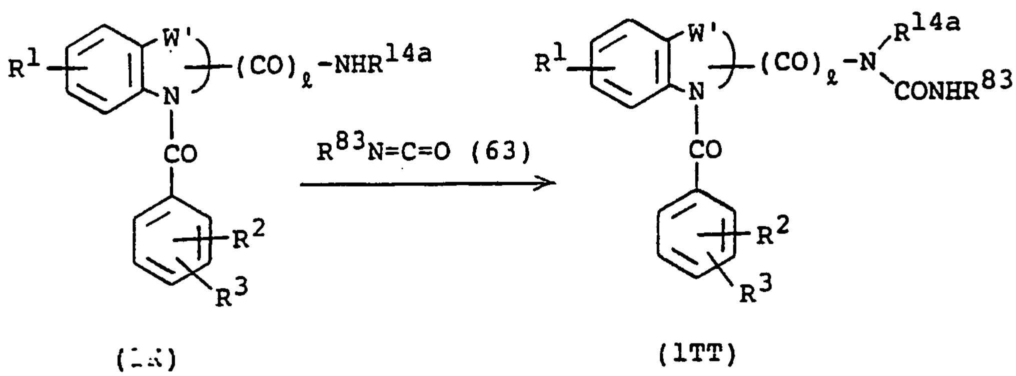
wherein R^1, R^2, R^3, and W' are as defined above, and R^{81} is hydroxyimino or a lower alkanoyloxyimino.

The reaction of converting the compound (1SS) into the compound (1ℓℓ) is carried out by catalytically hydrogenating the compound (1SS) in an appropriate solvent in the presence of a catalyst. The solvent includes, for example, water, acetic acid, alcohols (e.g. methanol, ethanol, isopropanol, etc.), hydrocarbons (e.g. hexane, cyclohexane, etc.), ethers (e.g. diethylene glycol dimethyl ether, dioxane, tetrahydrofuran, diethyl ether, etc.), esters (e.g. ethyl acetate, methyl acetate, etc.), aprotic polar solvents (e.g. dimethylformamide, etc.), or a mixture of these solvents. The catalyst includes, for example, palladium, palladium black, palladium-carbon, platinum, platinum oxide, copper chromate, Raney nickel, and the like. The catalyst is usually used in an amount of 0.02 to 1 part by weight to 1 part by weight of the compound (1SS). The reaction is usually carried out at a temperature of from

about -20°C to about 100°C, peferably about 0°C to about 70°C, under a hydrogen atmospheric pressure of 1 to 10 atm. for about 0.5 to 20 hours.

Alternatively, the reducing reaction can also be carried out by using a hydrogenating reducing agent. The hydrogenating reducing agent includes, for example, lithium aluminum hydride, sodium boro hydride, diborane, etc. The reducing agent is usually used in an amount of at least one mole, preferably 1 to 10 moles, to 1 mole of the compound (1SS). The reaction is usually carried out in an appropriate solvent, such as water, lower alcohols (e.g. methanol, ethanol, isopropanol, etc.), ethers (e.g. tetrahydrofuran, diethyl ether, diglyme, etc.), acetic acid, and the like, at a temperature of about 0°C to about 200°C, preferably about 0°C to 170°C, for about 10 minutes to about 10 hours. When lithium aluminum hydride or diborane is used as the reducing agent, it is preferable to use an anhydrous solvent such as diethyl ether, tetrahydrofuran, diglyme, etc.

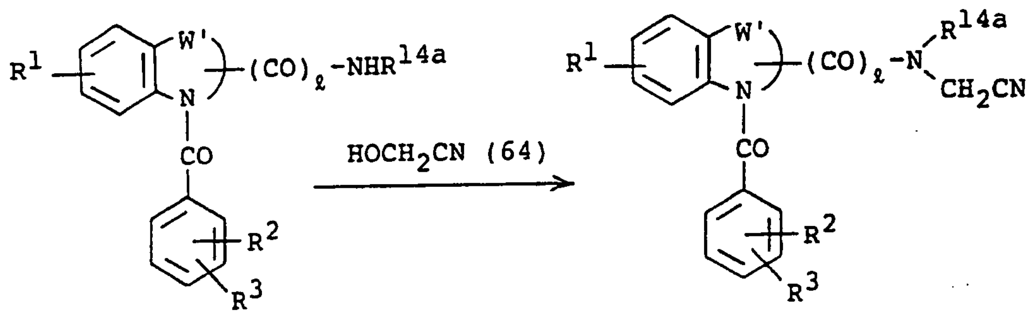
[Reaction Scheme-43]



wherein R^1, R^2, R^3, W', ℓ, R^{14a} are as defined above, and R^{83} is phenyl or a lower alkyl.

The reaction of the compound (1K) and the compound (63) can be carried out under the same conditions as in the reaction of the compound (2b) and the compound (38) in the above Reaction Scheme-26.

[Reaction Scheme-44]

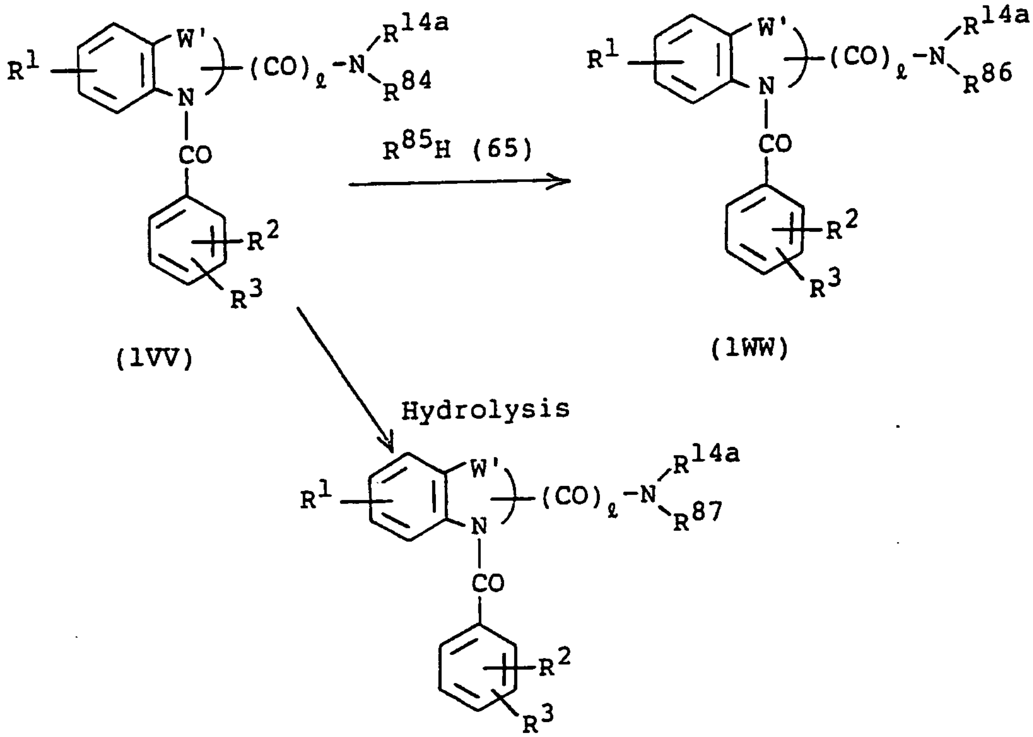


(1K) (1UU)

wherein R^1, R^2, R^3, W', ℓ, R^{14a} are as defined above.

The reaction of the compound (1K) and the glyconitrile (64) can be carried out in an appropriate solvent. The solvent includes the same solvent as used in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4. The reaction is usually carried out at a temperature of from about 0°C to about 150°C, preferably about 0°C to about 100°C, for about 1 to 10 hours. The glyconitrile (64) is used in an amount of at least 1 mole, preferably 1 to 2 moles, to 1 mole of the compound (1K).

[Reaction Sch ..-45]



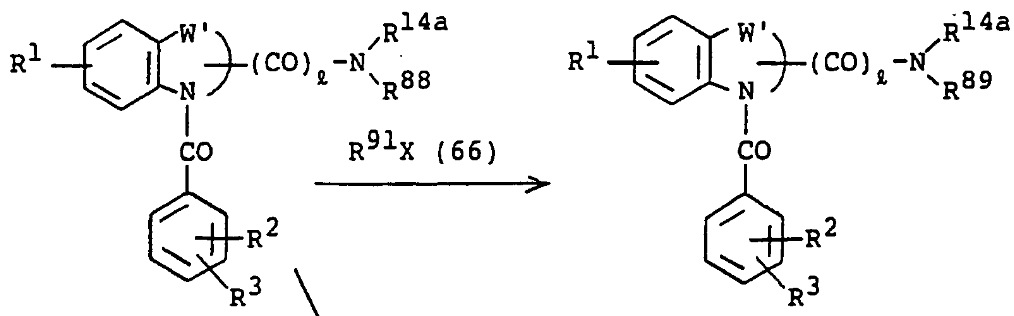
(1VV) (1WW) (1XX)

wherein R^1, R^2, R^3, W', ℓ, R^{14a} are as defined above, R^{84} is a lower alkoxycarbonyl-substituted lower alkyl, R^{85} is an amino having optionally a lower alkyl substituent, R^{86} is an aminocarbonyl-lower alkyl having optionally a lower alkyl substituent, and R^{87} is a carboxy-substituted lower alkyl.

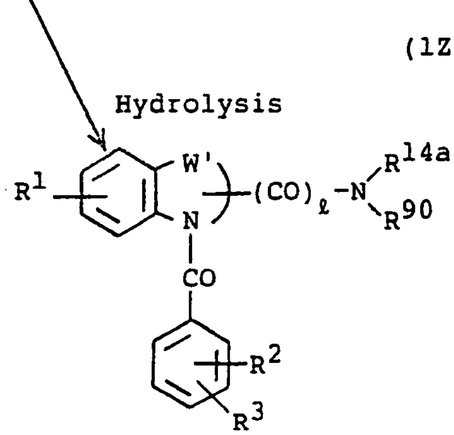
The reaction of the compound (1VV) and the compound (65) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The hydrolysis reaction of the compound (1.V) can be carried out under the same conditions as in the hydrolysis reaction of the compound (1QQ) and the compound (62) in the above Reaction Scheme-41.

[Reaction Scheme-46]



(1YY) (1ZZ)



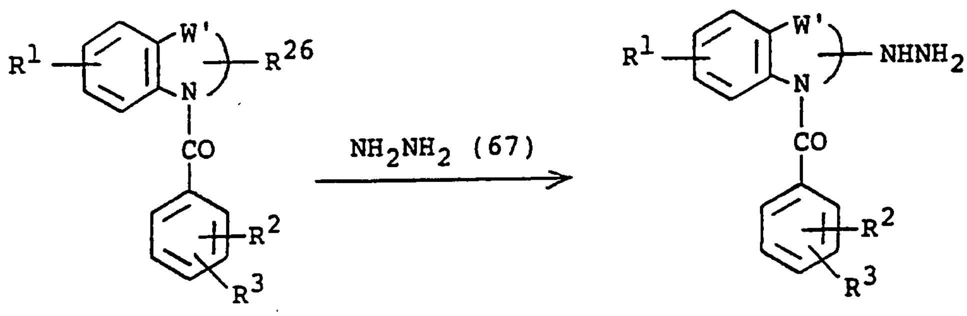
(1aaa)

wherein R^1, R^2, R^3, W', ℓ, X, and R^{14a} are as defined above, R^{88} is a tetrahydropyranyloxy-substituted lower alkyl, R^{89} is a lower alkanoyloxy-substituted lower alkyl, R^{90} is a hydroxy-substituted lower alkyl, and R^{91} is a lower alkanoyl.

The reaction of the compound (1YY) and the compound (66) can be carried out in a solvent such as acetic acid at a temperature of about 0°C to about 200°C, preferably about 0°C to about 150°C, for about 0.5 to 15 hours.

The hydrolysis reaction of the compound (1YY) can be carried out under the same conditions as in the hydrolysis reaction of the compound (1QQ) and the compound (62) in the above Reaction Scheme-41, wherein a pyridinium salt (e.g. pyridinium p-toluenesulfonate, etc.) may be used as the acid.

[Reaction Scheme-47]

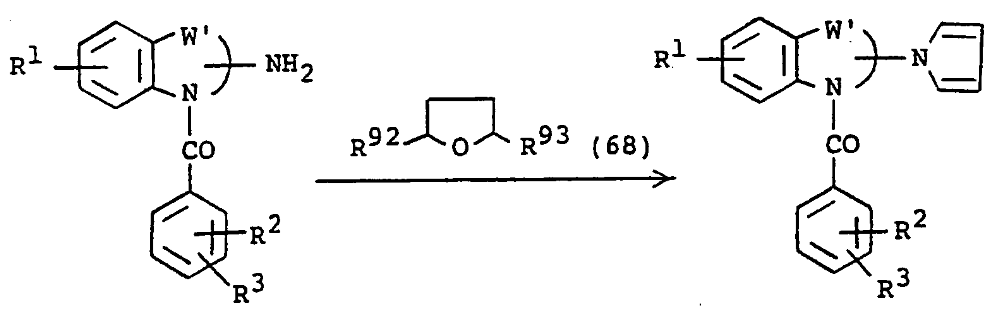


(1A) (1bbb)

wherein R^1, R^2, R^3, W', and R^{26} are as defined above.

The reaction of converting the compound (1A) into the compound (1bbb) can be carried out under the same conditions as in the reaction of converting the compound (1A) into the compound (1C) in the above Reaction Scheme-15.

[Reaction Scheme-48]



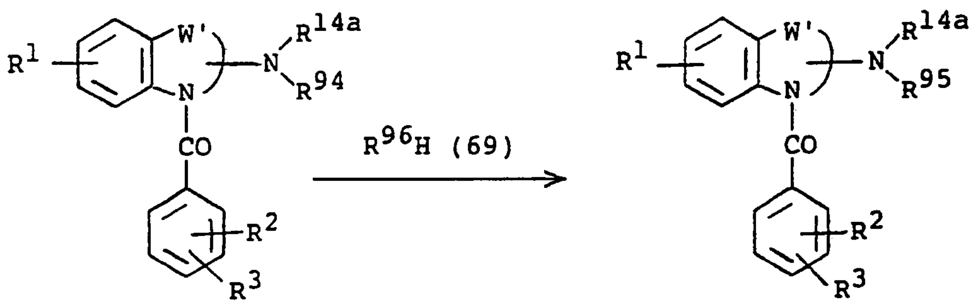
(1ℓℓ) (1ccc)

wherein R^1, R^2, R^3 and W' are as defined above, R^{92} and R^{93} are each a lower alkoxy.

The reaction of the compound (1ℓℓ) and the compound (68) is carried out in an appropriate solvent in the presence of an acid. The solvent includes, for example, water, alcohols (e.g. methanol, ethanol, isopropanol, etc.), ketones (e.g. acetone, methyl ethyl ketone, etc.), ethers (e.g. dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, etc.), fatty

acids (e.g. acetic acid, formic acid, etc.), or a mixture of these solvents. The acid includes, for example, mineral acids (e.g. hydrochloric acid, sulfuric acid, hydrobromic acid, etc.), organic acids (e.g. formic acid, acetic acid, aromatic sulfonic acids, etc.). The reaction is usually carried out at a temperature of from room temperature to about 200°C, preferably from room temperature to about 150°C, for about 0.5 to 5 hours. The compound (68) is usually used in an amount of at least 1 mole, preferably 1 to 2 moles, to 1 mole of the compound (1ℓℓ).

[Reaction Scheme-49]



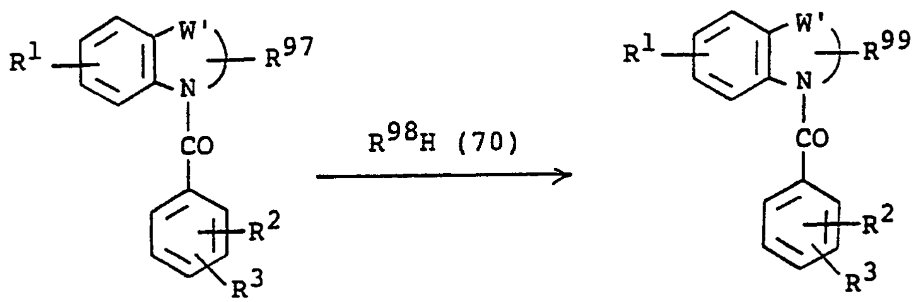
(1ddd) (1eee)

wherein R^1, R^2, R^3, W', and R^{14a} are as defined above, R^{94} is a halogen-substituted lower alkanoyl, R^{95} is an imidazolyl-substituted lower alkanoyl or an amino-lower alkanoyl having optionally a substituent selected from a lower alkyl and a lower alkoxycarbonyl, and R^{96} is imidazolyl, or an amino having optionally a substituent selected from a lower alkyl and a lower alkoxycarbonyl.

The reaction of the compound (1ddd) and the compound (69) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above

Reaction Scheme-4.

[Reaction Scheme-50]

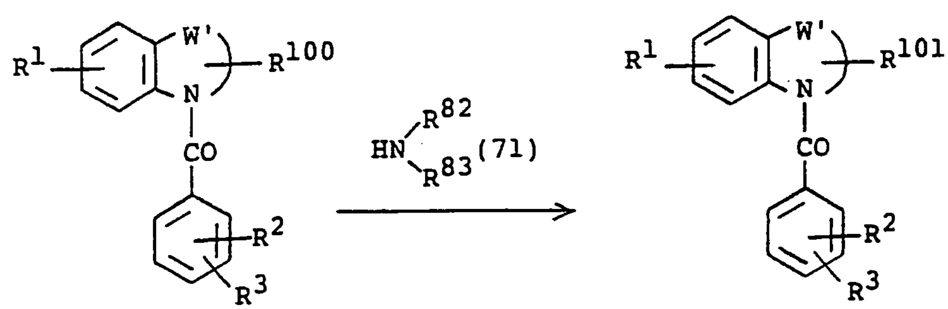


(1fff) (1ggg)

wherein R^1, R^2, R^3, and W' are as defined above, R^{97} is a lower alkanoyloxy having a halogen substituent, R^{98} is an amino having optionally a lower alkyl substituent, and R^{99} is an amino-lower alkanoyloxy having optionally a lower alkyl substituent.

The reaction of the compound (1fff) and the compound (70) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

[Reaction Scheme-51]



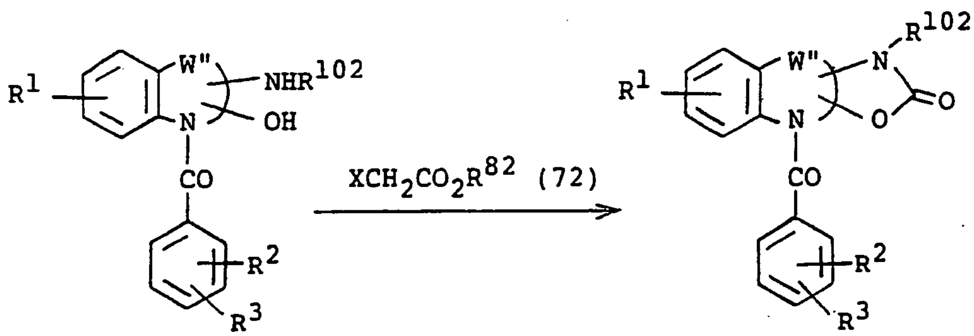
(1hhh) (1iii)

wherein R^1, R^2, R^3, W', R^{82}, and R^{83} are as defined above, R^{100} is a carboxy-substituted lower alkoxy, and R^{101} is a

group of the formula: $-O-A-CON\langle^{R^{82}}_{R^{83}}$ (A, R^{82} and R^{83} are as defined above).

The reaction of the compound (1hhh) and the compound (71) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

[Reaction Scheme-52]

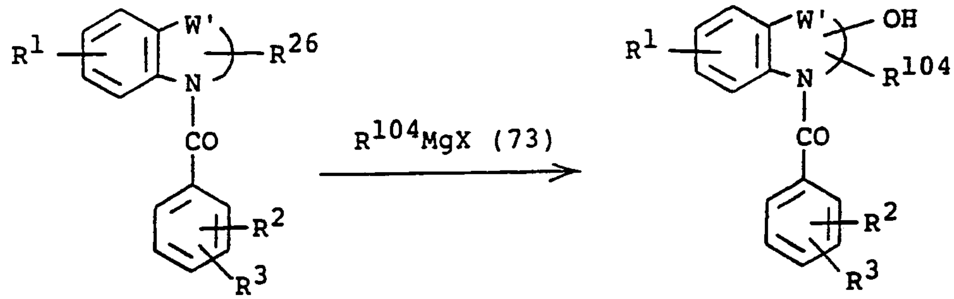


(1jjj) (1kkk)

wherein R^1, R^2, R^3, W", X, and R^{82} are as defined above, and R^{102} is hydrogen atom or a lower alkyl, provided that in the compound (1jjj), the groups of the formulae: $-NH-R^{102}$ and -OH are substituted at the positions adjacent each other.

The reaction of the compound (1jjj) and the compound (72) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

[Reaction Scheme-53]

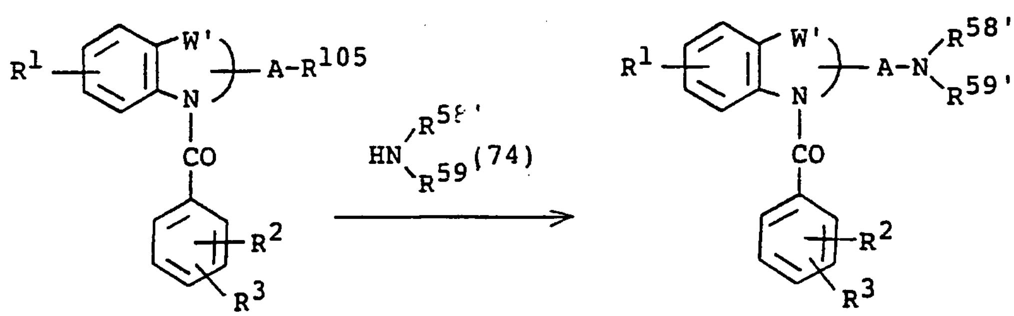


(1A) (1ℓℓℓ)

wherein R^1, R^2, R^3, W', R^{26} and X are as defined above, and R^{104} is a lower alkyl.

The reaction of the compound (1A) and the compound (73) can be carried out in an appropriate solvent. The solvent includes, for example, ethers (diethyl ether, dioxane, tetrahydrofuran, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), saturated hydrocarbons (e.g. pentane, hexane, heptane, cyclohexane, etc.), or a mixture of these solvents. The reaction is usually carried out at a temperature of from about -70°C to about 50°C, preferably from about -30°C to room temperature, for about 1 to 6 hours. The compound (73) is used in an amount of at least 1 mole, preferably 1 to 5 moles, to 1 mole of the compound (1A).

[Reaction Scheme-54]



(1mmm) (1nnn)

wherein R^1, R^2, R^3, W', $R^{58'}$, $R^{59'}$, and A are as defined above, and R^{105} is a lower alkylsulfonyloxy.

The reaction of the compound (1mmm) and the compound (74) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

Among the active compounds (1) of this invention, the compounds having an acidic group can easily be converted into salts by treating with a pharmaceutically acceptable basic compound. The basic compound includes, for example, metal hydroxides such as sodium hydroxide, potassium hydroxide, lithium hydroxide, calcium hydroxide, etc., alkali metal carbonates or hydrogen carbonates such as sodium carbonate, sodium hydrogen carbonate, etc., alkali metal alcoholates such as sodium methylate, potassium ethylate, etc. Besides, among the active compounds (1) of this invention, the compounds having a basic group can easily be converted into acid addition salts thereof by treating with a pharmaceutically acceptable acid. The acid includes, for example, inorganic acids such as sulfuric acid, nitric acid, hydrochloric acid, hydrobromic acid, etc., and organic acids such as acetic acid, p-toluenesulfonic acid, ethanesulfonic acid, oxalic acid, maleic acid, fumaric acid, citric acid, succinic acid, benzoic acid, etc. These salts are useful as an active ingredient as like as the compounds (1) in the free form.

In addition, the compounds (1) of this invention include stereoisomers and optical isomers, and these isomers are also useful as the active ingredient in this invention.

The compounds of this invention thus obtained can easily be isolated and purified by conventional isolation methods. The isolation methods are, for example, distillation method, recrystallization method, column chromatography, ion exchange chromatography, gel chromatography, affinity chromtography, preparative thin layer chromatography, extraction with a solvent, and the like.

The compounds and their salts of this invention are useful as a vasopressin antagonist and are used in the form of a conventional pharmaceutical preparation. The preparation is prepared by using conventional dilutents or carriers such as fillers, thickening agents, binders, wetting agents, disintegrators, surfactants, lubricants, and the like. The pharmaceutical preparations may be selected from various forms in accordance with the desired utilities, and the representative forms are tablets, pills, powders, solutions, suspensions, emulsions, granules, capsules, suppositories, injections (solutions, suspensions, etc.), and the like. In order to form in tablets, there are used carriers such as vehicles (e.g. lactose, white sugar, sodium chloride, glucose, urea, starches, calcium carbonate, kaolin, crystalline cellulose, silicic acid, etc.), binders (e.g. water, ethanol, propanol, simple syrup, glucose solution, starch solution, gelatin solution, carboxymethyl cellulose, shellac, methyl cellulose, potassium phosphate, polyvinylpyrrolidone, etc.), disintegrators (e.g. dry starch, sodium arginate, agar powder, laminaran powder, sodium hydrogen carbonate, calcium carbonate, polyoxyethylene sorbitan fatty acid esters, sodium laurylsulfate, stearic

monoglyceride, starches, lactose, etc.), disintegration inhibitors (e.g. white sugar, stearin, cacao butter, hydrogenated oils, etc.), absorption promoters (e.g. quaternary ammonium base, sodium laurylsulfate, etc.), wetting agents (e.g. glycerin, starches, etc.), adsorbents (e.g. starches, lactose, kaolin, bentonite, colloidal silicates, etc.), lubricants (e.g. purified talc, stearates, boric acid powder, polyethylene glycol, etc.), and the like. Moreover, the tablets may also be in the form of a conventional coated tablet, such as sugar-coated tablets, gelatin-coated tablets, enteric coated tablets, film coating tablets, or double or multiple layer tablets. In the preparation of pills, the carriers include vehicles (e.g. glucose, lactose, starches, cacao butter, hydrogenated vegetable oils, kaolin, talc, etc.), binders (e.g. gum arabic powder, tragacanth powder, gelatin, ethanol, etc.), disintegrators (e.g. laminaran, agar, etc.), and the like. In the preparation of suppositories, the carriers include, for example, polyethylene glycol, cacao butter, higher alcohols, higher alcohol esters, gelatin, semi-synthetic glycerides, and the like. Capsules can be prepared by charging a mixture of the compound of this invention with the above carriers into hard gelatin capsules or soft capsules in a usual manner. In the preparation of injections, the solutions, emulsions or suspendions are sterilized and are preferably made isotonic with the blood. In the preparation of these solutions, emulsions and suspensions, there are used conventional diluents, such as water, ethyl alcohol, macrogol

(propylene glycol), ethoxylated isostearyl alcohol, polyoxylated isostearyl alcohol, polyoxyethylene sorbitan fatty acid esters, and the like. In this case, the pharmaceutical preparations may also be incorporated with sodium chloride, glucose, or glycerin in an amount sufficient to make them isotonic, and may also be incorporated with conventional solubilizers, buffers, anesthetizing agents. Besides, the pharmaceutical preparations may optionally be incorporated with coloring agents, preservatives, perfumes, flavors, sweeting agents, and other medicaments, if required.

The amount of the active compound of this invention (active ingredient) to be incorporated into the anti-vasopressin preparations is not specified but may be selected from a broad range, but usually, it is preferably in the range of 1 to 70 % by weight, more preferably 5 to 50 % by weight.

The anti-vasopressin preparation of this invention may be administered in any method, and suitable method for administration may be determined in accordance with various forms of preparation, ages, sexes and other conditions of the patients, the degree of severity of diseases, and the like. For instance, tablets, pills, solutions, suspensions, emulsions, granules and capsules are administered orally. The injections are intraveneously administered alone or together with a conventional auxiliary liquid (e.g. glucose, amino acid solutions), and further are optionally administered alone in intramuscular, intracutaneous, subcutaneous, or intraperitoneal route, if required. Suppositories are

administered in intrarectal route.

The dosage of the anti-vasopressin agent of this invention may be selected in accordance with the usage, ages, sexes and other conditions of the patients, the degree of severity of the diseases, and the like, but is usually in the range of about 0.6 to 50 mg of the active compound of this invention per 1 kg of body weight of the patient per day. The active compound is preferably contained in an amount of 10 to 1000 mg per the dosage unit.

Brief Description of Drawing

Fig. 1 to Fig. 4 show a chart of NMR ($CDCl_3$) of the compounds in Examples 978 and 979.

Best Mode for Carrying Out the Invention

The present invention is illustrated by the following Preparations of anti-vasopressin agent, Reference Examples of processes for preparing the starting compounds to be used for preparing the active compounds, Examples of processes for preparing the active compounds, and Experiments of the activities of the active compounds of this invention.

Preparation 1

Film coated tablets are prepared from the following components.

Components	Amount
4-Methylamino-1-[4-(3,5-dichlorobenzoyl-amino)benzoyl]-1,2,3,4-tetrahydroquinoline	150 g

Avicel (tradename of microcrystalline cellulose, manufactured by Asahi Chemical Industry Co., Ltd., Japan)	40 g
Corn starch	30 g
Magnesium stearate	2 g
Hydroxypropyl methylcellulose	10 g
Polyethylene glycol-6000	3 g
Castor oil	40 g
Ethanol	40 g

The active component of this invention, Avicel, corn starch and magnesium stearate are mixed and kneaded and the mixture is tabletted using a conventional pounder (R 10 mm) for sugar coating. The tablets thus obtained are coated with a film coating agent consisting of hydroxypropyl methylcellulose, polyethylene glycol-6000, castor oil and ethanol to give film coated tablets.

Preparation 2

Tablets are prepared from the following components.

Components	Amount
1-[4-(N-Butylanilinoacetylamino)benzoyl]-2,3,4,5-tetrahydroy-1H-benzazepine	150 g
Citric acid	1.0 g
Lactose	33.5 g
Dicalcium phosphate	70.0 g
Pullonic F-68	30.0 g
Sodium laurylsulfate	5.0 g
Polyvinylpyrrolidone	[illegible].0 g
Polyethylene glycol (Carbowax 1500)	4.5 g

Polyethylene glycol (Carbowax 6000)	45.0 g
Corn starch	30.0 g
Dry sodium stearate	3.0 g
Dry magnesium stearate	3.0 g
Ethanol	q.s.

The active compound of this invention, citric acid, lactose, dicalcium phosphate, Pullonic F-68 and sodium laurylstearate are mixed. The mixture is screened with No. 60 screen and is granulated with an alcohol solution containing polyvinylpyrrolidone, carbowax 1500 and 6000. If required, an alcohol is added thereto so that the powder mixture is made a paste-like mass. Corn starch is added to the mixture and the mixture is continuously mixed to form uniform particles. The resulting particles are passed through No. 10 screen and entered into a tray and then dried in an oven at 100°C for 12 to 14 hours. The dried particles are screened with No. 16 screen and thereto are added dry sodium laurylsulfate and dry magnesium stearate, and the mixture is tabletted to form the desired shape.

The core tablets thus prepared are vanished and dusted with talc in order to guard from wetting. Undercoating is applied to the core tablets. In order to administer the tablets orally, the core tablets are vanished several times. In order to give round shape and smooth surface to the tablets, further undercoating and coating with lubricant are applied thereto. The tablets are further coated with a coloring coating material until the desired

colored tablets are obtained. After drying, the coated tablets are polished to obtain the desired tablets having uniform gloss.

Preparation 3

An injection preparation is prepared from the following components.

Components	Amount
4-Methyl-1-[4-(2,3-dimethylbenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine	5 g
Polyethylene glycol (molecular weight: 4000)	0.3 g
Sodium chloride	0.9 g
Polyoxyethylene sorbitan monooleate	0.4 g
Sodium metabisulfite	0.1 g
Methyl-paraben	0.18 g
Propyl-paraben	0.02 g
Distilled water for injection	10.0 ml

The above parabens, sodium metabisulfite and sodium chloride are dissolved in distilled water of half volume of the above with stirring at 80°C. The solution thus obtained is cooled to 40°C, and the active compound of this invention and further polyethylene glycol and polyoxyethylene sorbitan monooleate are dissolved in the above solution. To the solution is added distilled water for injection to adjust to the desired volume, and the solution i[illegible]terilized by filtering with an appropriate filter pa[illegible]er to give an injection preparation.

Reference Example 1

To a solution of 1,2,3,4-tetrahydroquinoline (28.7 g) in acetone (400 ml) and water (200 ml) is added potassium carbonate (38.8 g), and thereto is added p-nitrobenzoyl chloride (40 g) under ice-cooling and the mixture is stirred at room temperature overnight. To the reaction mixture is added a suitable amount of water. The precipitated crystal is collected by filtration and dried to give 1-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline (40.8 g) as white powder, m.p. 86 - 88°C.

Reference Example 2

To a solution of 10 % Pd-C (5 g) in ethanol (500 ml) is added 1-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline (53.4 g) and the mixture is subjected to catalytic reduction at ordinary temperature under atmospheric pressure of hydrogen. After the reduction, 10 % Pd-C is removed by filtration, and the filtrate is concentrated under reduced pressure to give 1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline (46.7 g) as yellow powder, m.p. 185 - 188°C.

Reference Example 3

Using the suitable starting materials, the following compounds are obtained in the same manner as in Reference Example 1.

1-(3-Nitrobenzoyl)-1,2,3,4-tetrahydroquinoline, white powder, m.p. 134 - 136°C

1-(2-Nitrobenzoyl)-1,2,3,4-tetrahydroquinoline,

yellow powder, m.p. 152 - 154°C

3-Methyl-1-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 109 - 110°C

4-Methyl-1-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 134 - 136°C

2-Methyl-1-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 143 - 145°C

1-(4-Nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, yellow powder, m.p. 143 - 145°C

1-(3-Methyl-4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 100 - 102°C

1-(3-Methoxy-4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, yellow powder, m.p. 146 - 148°C

1-(4-Nitrobenzoyl)-1,2,3,4,5,6-hexahydrobenzazocine, white powder, m.p. 83 - 85°C

1-(4-Nitrobenzoyl)-3,4-dihydro-2H-1,4-benzoxazine, yellow powder, m.p. 167 - 169°C

1-(4-Nitrobenzoyl)-1,2,3,5-tetrahydro-4,1-benzoxazepine, yellow powder, m.p. 196 - 198°C

1-(4-Nitrobenzoyl)-4-methyl-1,2,3,4-tetrahydroquinoxaline, brown powder

^{1}H-NMR ($CDCl_3$) δ : 3.03 (3H, s), 3.54 (2H, t, J=5.7 Hz), 4.06 (2H, t, J=5.7 Hz), 6.2-6.5 (2H, m), 6.70 (1H, d, J=8.2 Hz), 6.9-7.1 (1H, m), 7.54 (2H, d, J=8.8 Hz), 8.13 (2H, d, J = 8.8 Hz)

1-(4-Nitrobenzoyl)-5-methyl-2,3,4,5-tetrahydro-1H-

1,5-benzodiazepine, yellow oil

^{1}H-NMR ($CDCl_3$) δ : 1.7-2.0 (1H, m), 2.0-2.3 (1H, m), 2.8-3.0 (1H, m), 2.98 (3H, s), 3.0-3.2 (1H, m), 3.4-3.6 (1H, m), 4.6-4.8 (1H, m), 6.5-6.7 (2H, m), 6.94 (1H, d, J=8.1 Hz), 7.1-7.2 (1H, m), 7.33 (2H, d, J=8.9 Hz), 7.97 (2H, d, J=8.9 Hz)

1-(4-Nitrobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, brown oil

^{1}H-NMR ($CDCl_3$) δ : 2.44 (3H, s), 3.0-3.3 (3H, m), 3.77 (1H, d, J=13.7 Hz), 4.06 (1H, d, J=13.6 Hz), 4.9-5.1 (1H, m), 6.59 (1H, d, J=7.7 Hz), 6.97 (1H, t, J=7.6 Hz), 7.15 (1H, t, J=7.4 Hz), 7.2-7.5 (3H, m), 8.03 (2H, d, J=8.8 Hz)

1-(3-Methoxy-4-nitrobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow powder, m.p. 146 - 148°C

1-(4-Nitrobenzoyl)-4-n-propyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow powder, m.p. 131 - 133°C

1-(4-Nitrobenzoyl)-5-chloro-1,2,3,4-tetrahydroquinoline, white powder, m.p. 134 - 136°C

1-(4-Nitrobenzoyl)-6-methoxy-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 149 - 151°C

1-(4-Nitrobenzoyl)-6-methyl-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 109 - 110°C

1-(4-Nitrobenzoyl)-7-methoxy-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 139 - 141°C

1-(4-Nitrobenzoyl)-3-(4-methyl-1-piperazinyl)-1,2,3,4-tetrahydroquinoline, yellow amorphous

^{1}H-NMR ($CDCl_3$) δ : 2.29 (3H, s), 2.35-3.20 (11H, m), 3.86-4.15 (2H, m), 6.48-6.63 (1H, m), 6.89 (1H, t, J=7.4 Hz), 7.05 (1H, t, J=7.4 Hz), 7.22 (1H, d, J=7.4 Hz), 7.52 (2H, d, J=8.8 Hz), 8.11 (2H, d, J=8.8 Hz)

1-(4-Nitrobenzoyl)-3-(1-pyrrolidinyl)-1,2,3,4-tetrahydroquinoline, yellow amorphous

^{1}H-NMR ($CDCl_3$) δ : 1.70-1.95 (4H, m), 2.52-3.30 (7H, m), 3.80-4.22 (2H, m), 6.52 (1H, brs), 6.88 (1H, t, J=7.6 Hz), 6.96-7.11 (1H, m), 7.20 (2H, d, J=7.6 Hz), 7.54 (2H, d, J=8.8 Hz), 8.12 (2H, d, J=8.8 Hz)

1-(4-Nitrobenzoyl)-4-oxo-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 189 - 190°C

1-(4-Nitrobenzoyl)-3-hydroxymethyl-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 97 - 100°C

1-(4-Nitrobenzoyl)-3-ethoxycarbonyl-1,2,3,4-tetrahydroquinoline, pale yellow powder, m.p. 162 - 163°C

1-(4-Nitrobenzoyl)-4-dimethylamino-1,2,3,4-tetrahydroquinoline, light brown oil

^{1}H-NMR ($CDCl_3$) δ : 1.80-2.02 (1H, m), 2.20-2.50 (7H, m), 3.47 (1H, t, J=4.9 Hz), 3.70-3.88 (1H, m), 4.06-4.25 (1H, m), 6.46 (1H, d, J=7.5 Hz), 6.89 (1H, t, J=7.5 Hz), 7.05 (1H, t, J=7.5 Hz), 7.34 (1H, d, J=7.5 Hz), 7.50 (2H, d, J=7.0 Hz), 8.10 (2H, d, J=7.0 Hz)

Reference Example 4

Using the suitable starting materials, the following compounds are obtained in the same manner as in Reference Example 2.

1-(3-Aminobenzoyl)-1,2,3,4-tetrahydroquinoline, white powder, m.p. 128 - 130°C

1-(2-Aminobenzoyl)-1,2,3,4-tetrahydroquinoline, yellow powder

^{1}H-NMR ($CDCl_3$) δ : 2.01 (2H, quint, J=6.6 Hz), 2.81 (2H, t, J=6.6 Hz), 3.86 (2H, t, J=6.4 Hz), 4.6-4.8 (2H, m), 6.43 (1H, t, J=7 Hz), 6.66 (1H, d, J=8 Hz), 6.79 (1H, dd, J=1.4 Hz, J=7.6 Hz), 6.8-7.2 (5H, m)

3-Methyl-1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 197 - 200°C

4-Methyl-1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 197 - 199°C

2-Methyl-1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 204 - 206°C

1-(4-Aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, yellow powder, m.p. 172 - 174°C

1-(3-Methyl-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 156 - 158°C

1-(3-Methoxy-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 165 - 167°C

1-(4-Aminobenzoyl)-1,2,3,4,5,6-hexahydrobenzazocine, white powder, m.p. 177 - 179°C

1-(4-Aminobenzoyl)-3,4-dihydro-2H-1,4-benzoxazine,

white powder, m.p. 192 - 194°

1-(4-Aminobenzoyl)-1,2,3,5-tetrahydro-4,1-benzoxazepine, yellow powder, m.p. 196 - 198°C

1-(4-Aminobenzoyl)-4-methyl-1,2,3,4-tetrahydroquinoxaline, yellow powder, m.p. 210 - 212°C

1-(4-Aminobenzoyl)-5-methyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine, white powder, m.p. 159 - 161°C

1-(4-Aminobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, brown powder, m.p. 169 - 171°C

1-(3-Methoxy-4-aminobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow oil

^{1}H-NMR ($CDCl_3$) δ : 2.41 (3H, s), 2.9-3.2 (3H, m), 3.61 (3H, s), 3.6-4.2 (4H, m), 4.8-5.2 (1H, m), 6.38 (1H, d, J=8.1 Hz), 6.6-6.8 (3H, m), 6.9-7.2 (2H, m), 7.2-7.4 (1H, m)

1-(4-Aminobenzoyl)-4-n-propyl-2,3,4,5-tetrahydro-1H-1,4-benzazepine, brown powder, m.p. 151 - 153°C

1-(4-Aminobenzoyl)-5-chloro-1,2,3,4-tetrahydroquinoline, white powder, m.p. 174 - 175°C

1-(4-Aminobenzoyl)-6-methoxy-1,2,3,4-tetrahydroquinoline, pale yellow powder, m.p. 159 - 160°C

1-(4-Aminobenzoyl)-6-methyl-1,2,3,4-tetrahydroquinoline, white powder, m.p. 145 - 146°C

1-(4-Aminobenzoyl)-7-methoxy-1,2,3,4-tetrahydroquinoline, pale yellow powder, m.p. 150 - [illegible]°C

1-(4-Aminobenzoyl)-3-(4-methyl-1-piperazinyl)-1,2,3,4-tetrahydroquinoline, light beige powder, m.p. 157 -

159°C

1-(4-Aminobenzoyl)-3-(1-pyrrolidinyl)-1,2,3,4-tetrahydroquinoline, pale yellow powder, m.p. 173 - 174.5°C

1-(4-Aminobenzoyl)-2,3-dihydro-4(1H)-quinolinone, pale yellow powder, m.p. 178 - 180°C

1-(4-Aminobenzoyl)-3-hydroxymethyl-1,2,3,4-tetrahydroquinoline, white powder, m.p. 179 - 181°C

1-(4-Aminobenzoyl)-3-ethoxycarbonyl-1,2,3,4-tetrahydroquinoline, pale yellow amorphous

^{1}H-NMR ($CDCl_3$) δ : 1.21 (3H, t, J=7.1 Hz), 3.00-3.24 (3H, m), 3.70-4.30 (6H, m), 6.48 (2H, d, J=8.5 Hz), 6.69 (1H, d, J=7.9 Hz), 6.77-7.30 (5H, m)

1-(4-Aminobenzoyl)-4-dimethylamino-1,2,3,4-tetrahydroquinoline, brown oil

^{1}H-NMR ($CDCl_3$) δ : 1.83-2.05 (1H, m), 2.13-2.30 (1H, m), 2.34 (6H, m), 3.55-3.83 (2H, m), 3.89 (1H, brs), 3.97-4.18 (1H, m), 6.47 (2H, d, J=7.0 Hz), 6.68 (1H, d, J=7.9 Hz), 6.85-7.05 (2H, m), 7.20 (2H, d, J=7.0 Hz), 7.37 (1H, d, J=7.4 Hz)

Reference Example 5

To terephthalic acid monomethyl ester (15 g) is added thionyl chloride (100 ml) and the mixture is refluxed for 2 hours. The thionyl chloride is distilled off under reduced pressure to give terephthalic acid chloride monomethyl ester. Separately, to a solution of 1,2,3,4-tetrahydroquinoline (14.4 g) in dichloromethane (200 ml) is

added triethylamine (16.9 g) and further thereto is added slowly terephthalic acid chloride monomethyl ester obtained above under ice-cooling. Then, the mixture is stirred at room temperature for 1 hour. After completion of the reaction, water is added to the reaction mixture. The mixture is extracted with dichloromethane and dried over magnesium sulfate. The solvent is distilled off under reduced pressure and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane) to give 1-(4-methoxycarbonylbenzoyl)-1,2,3,4-tetrahydroquinoline (22.7 g) as white powder, m.p. 72 - 74°C.

Reference Example 6

To a solution of 1-(4-methoxycarbonylbenzoyl)-1,2,3,4-tetrahydroquinoline (22.7 g) in methanol (300 ml) is added 5 % aqueous sodium hydroxide solution (150 ml) and the mixture is refluxed for 2 hours. Methanol is distilled off under reduced pressure and the resulting residue is acidified with diluted hydrochloric acid, extracted with diethyl ether, and dried over magnesium sulfate. The solvent is distilled off under reduced pressure and the resulting crystal is collected by filtration to give 1-(4-carboxybenzoyl)-1,2,3,4-tetrahydroquinoline (13.2 g) as white powder, m.p. 181 - 183°C.

Reference Example 7

Using the suitable starting materials, the

following compounds are obtained in the same manner as in Reference Example 1.

5-Dimethylamino-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, pale yellow powder, m.p. 139 - 142°C

5-Dimethylamino-1-(3-methoxy-4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 139 - 141°C

4-(N-Methyl-N-ethylamino)-1-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline, pale yellow oil

^{1}H-NMR ($CDCl_3$) δ : 1.11 (3H, t, J=7.1 Hz), 1.90-2.25 (2H, m), 2.30 (3H, s), 2.57 (2H, q, J=7.1 Hz), 3.55-3.85 (2H, m), 4.00-4.21 (1H, m), 6.35-6.60 (1H, m), 6.80-6.98 (1H, t, J=7.9 Hz), 7.00-7.15 (1H, m), 7.33-7.60 (3H, m), 8.10 (2H, d, J=8.8 Hz)

4-Dimethylamino-1-(3-methoxy-4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline, brown oil

^{1}H-NMR ($CDCl_3$) δ : 1.80-2.05 (1H, m), 2.33 (6H, s), 2.30-2.50 (1H, m), 3.40-3.52 (1H, m), 3.78 (3H, s), 3.70-3.88 (1H, m), 4.04-4.24 (1H, m), 6.52 (1H, d, J=8.2 Hz), 6.85-7.13 (4H, m), 7.28-7.38 (1H, m), 7.71 (1H, d, J=8.2 Hz)

1-(4-Nitrobenzoyl)-4-ethyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow oil

^{1}H-NMR ($CDCl_3$) δ : 1.16 (3H, t, J=7.1 Hz), 2.5-2.7 (2H, m), 3.0-3.3 (3H, m), 3.98 (2H, q, J=14 Hz), 4.8-5.0 (1H, m), 6.59 (1H, d, J=7.7 Hz), 6.96 (1H, t, J=7.7 Hz),

7.14 (1H, t, J=7.4 Hz), 7.2-7.4 (3H, m), 8.02 (2H, d, J=8.8 Hz)

1-(4-Nitrobenzoyl)-4-isopropyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow powder, m.p. 222 - 223°C

1-(4-Nitrobenzoyl)-4-cyclohexyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, brown oil

^{1}H-NMR ($CDCl_3$) δ : 1.0-1.5 (5H, m), 1.5-2.1 (5H, m), 2.4-2.7 (1H, m), 2.9-3.3 (3H, m), 3.94 (2H, s), 4.9-5.1 (1H, m), 6.57 (1H, d, J=7.7 Hz), 6.8-7.0 (1H, m), 7.0-7.2 (1H, m), 7.2-7.4 (3H, m), 8.01 (2H, d, J=8.8 Hz)

1-(4-Nitrobenzoyl)-5-methyl-1,2,3,4,5,6-hexahydro-1,5-benzodiazocine, yellow oil

^{1}H-NMR ($CDCl_3$) δ : 1.5-2.1 (2H, m), 2.40 (3H, s), 2.3-2.6 (1H, m), 2.8-3.2 (2H, m), 3.50 (1H, d, J=13.4 Hz), 3.84 (1H, d, J=13.4 Hz), 4.8-5.0 (1H, m), 7.0-7.3 (4H, m), 7.41 (2H, d, J=8.9 Hz), 8.00 (2H, d, J=8.9 Hz)

1-(4-Nitrobenzoyl)-1,2,3,4-tetrahydro-5,1-benzoxazepine, white powder, m.p. 144.5 - 145.5°C

1-(2-Nitrobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow powder, m.p. 177 - 180°C

1-(3-Nitrobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow powder, m.p. 145 - 146°C

6-Fluoro-1-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline, yellow needles, m.p. 145 - 146°C

Reference Example 8

Using the suitable starting materials, the

following compounds are obtained in the same manner as in Reference Example 2.

5-Dimethylamino-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 120 - 122°C

5-Dimethylamino-1-(3-methoxy-4-amino)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 121 - 123°C

4-(N-Methy-N-ethylamino)-1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline, orange amorphous

^{1}H-NMR ($CDCl_3$) δ : 1.11 (3H, t, J=7.1 Hz), 1.90-2.20 (2H, m), 2.28 (3H, s), 2.26 (2H, q, J=7.1 Hz), 3.60-4.25 (5H, m), 6.48 (2H, d, J=8.5 Hz), 6.69 (1H, d, J=7.9 Hz), 6.80-7.05 (2H, m), 7.24 (2H, d, J=8.5 Hz), 7.46 (1H, d, J=6.2 Hz)

4-Dimethylamino-1-(3-methoxy-4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline, pale yellow amorphous

^{1}H-NMR ($CDCl_3$) δ : 1.83-2.04 (1H, m), 2.15-2.32 (1H, m), 2.33 (6H, s), 3.50-3.82 (2H, m), 3.64 (3H, s), 3.95-4.18 (3H, m), 6.50 (1H, d, J=7.9 Hz), 6.65 (1H, dd, J=7.9 Hz, 1.1 Hz), 6.78-7.03 (4H, m), 7.34 (1H, dd, J=7.5 Hz, 1.5 Hz)

1-(4-Aminobenzoyl)-4-ethyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, white powder, m.p. 186 - 188°C

1-(4-Aminobenzoyl)-4-isopropyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, white powder, m.p. 191 - 192°C

1-(4-Aminobenzoyl)-4-cyclohexyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, white powder, m.p. 149.5 - 150.5°C

1-(4-Aminobenzoyl)-5-methyl-1,2,3,4,5,6-hexahydro-1,5-benzodiazocine, yellow powder, m.p. 143 - 145°C

1-(4-Aminobenzoyl)-1,2,3,4-tetrahydro-5,1-benzoxazepine, yellow powder, m.p. 163.5 - 164.5°C

1-(2-Aminobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow powder, m.p. 144 - 146°C

1-(3-Aminobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, white powder, mp. 153 - 155°C

6-Fluoro-1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline, white powder, m.p. 160.5 - 161.5°C

Reference Example 9

Using the suitable starting materials, the following compounds are obtained in the same manner as in Reference Example 1.

1-(2-Chloro-4-nitrobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine

^{1}H-NMR ($CDCl_3$) δ : 2.40 (3H, s), 2.96-3.33 (3H, m), 3.60-3.79 (1H, m), 3.96-4.23 (1H, m), 4.70-4.91 (1H, m), 6.80-7.43 (5H, m), 7.80-7.99 (1H, m), 8.08-8.21 (1H, m)

1-(3-Methyl-4-nitrobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine

^{1}H-NMR ($CDCl_3$) δ : 2.43 (3H, s), 2.48 (3H, s), 2.92-3.28 (3H, m), 3.91 (2H, AB-q, J=13.9 Hz, 45.5 Hz), 4.77-5.01 (1H, m), 6.54-6.70 (1H, m), 6.88-7.37 (5H, m), 7.62-7.78 (1H, m)

5-Dimethylamino-1-(2-chloro-4-nitrobenzoyl)-

2,3,4,5-tetrahydro-1H-benzazepine

^{1}H-NMR ($CDCl_3$) δ : 1.23-2.57 (10H, m), 2.68-5.15 (3H, m), 6.79-7.45 (4H, m), 7.49-8.39 (3H, m)

5-Oxo-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder (ethyl acetate/n-hexane), m.p. 147 - 148°C

5-Hydroxy-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder (ethyl acetate/n-hexane), m.p. 148 - 150°C

5-Methoxy-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless amorphous

^{1}H-NMR ($CDCl_3$) δ : 1.47-2.48 (4H, m), 2.70-3.10 (1H, m), 3.26-3.64 (3H, m), 4.29-5.12 (2H, m), 6.60 (1H, d, J=7.7 Hz), 6.88-7.67 (5H, m), 7.92-8.12 (2H, m)

5-Ethoxycarbonylmethoxy-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 107 - 108°C (recrystallized from ethyl acetate/n-hexane)

5-(4-Bromobutoxy)-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless oil

^{1}H-NMR ($CDCl_3$) δ : 1.49-2.55 (8H, m), 2.72-3.07 (1H, m), 3.24-3.77 (4H, m), 4.40-5.15 (2H, m), 6.53-6.66 (1H, m), 6.91-7.06 (1H, m), 7.07-7.80 (4H, m), 7.94-8.13 (2H, m)

5-(4-Dimethylaminobutoxy)-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless oil

^{1}H-NMR ($CDCl_3$) δ : 1.51-1.88 (6H, m), 2.23-2.61

(4H, m), 2.27 (3H, s), 2.35 (3H, s), 2.74-3.14 (1H, m), 3.55-3.77 (2H, m), 4.48-5.11 (2H, m), 6.54-6.66 (1H, m), 6.91-7.04 (1H, m), 7.06-7.80 (4H, m), 7.93-8.11 (2H, m)

5-[4-(Phthalimid-1-yl)propoxy-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless amorphous

^{1}H-NMR ($CDCl_3$) δ : 1.48-2.56 (6H, m), 2.71-3.05 (1H, m), 3.40-4.05 (4H, m), 4.47-5.11 (2H, m), 6.50-6.64 (1H, m), 6.84-7.03 (1H, m), 7.03-7.20 (1H, m), 7.20-7.57 (2H, m), 7.57-7.93 (5H, m), 7.97-8.20 (2H, m)

5-Chloro-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, light brown powder

^{1}H-NMR ($CDCl_3$) δ : 1.75-3.3 (4H, m), 4.6-6.25 (3H, m), 6.45-6.7 (1H, m), 6.8-7.5 (4H, m), 7.55-7.7 (1H, m), 7.9-8.1 (2H, m)

5-Oxo-1-(2-chloro-4-nitorobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, pale yellow amorphous

^{1}H-NMR ($CDCl_3$) δ : 1.95-2.45 (2H, m), 2.94 (1H, t, J=6 Hz), 3.05-5.3 (2H, m), 6.96-7.1 (1H, m), 7.12-7.5 (3H, m), 7.75-7.85 (1H, m), 7.95-8.1 (1H, m), 8.14 (1H, s)

4-Dimethylaminomethyl-1-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline, white powder, m.p. 117 - 119°C

3-Dimethylamino-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, yellow oil

^{1}H-NMR ($CDCl_3$) δ : 1.5-1.7 (1H, m), 2.1-2.4 (1H, m), 2.42 (6H, s), 2.6-2.7 (1H, m), 2.8-3.0 (3H, m,, 5.1-5.3 (1H, m), 6.62 (1H, d, J=7.8 Hz), 6.95 (1H, t, J=7.7 Hz),

7.14 (1H, t, J=7.5 Hz), 7.2-7.4 (3H, m), 8.00 (2H, d, J=8.9 Hz)

3-Dimethylamino-1-(3-methoxy-4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, yellow oil

^{1}H-NMR ($CDCl_3$) δ : 1.5-1.7 (1H, m), 2.0-2.3 (1H, m), 2.41 (6H, s), 2.5-2.8 (1H, m), 2.8-3.0 (3H, m), 3.75 (3H, s), 5.1-5.3 (1H, m), 6.6-6.8 (2H, m), 6.9-7.3 (4H, m), 7.59 (1H, d, J=8.3 Hz)

4-(4-Nitrobenzoyl)-3,4-dihydro-2H-1,4-benzothiazine, yellow powder, m.p. 180 - 182°C

5-(4-Nitrobenzoyl)-2,3,4,5-tetrahydro-1,5-benzothiazepine, yellow powder, m.p. 162 - 163°C

Reference Example 10

Using the suitable starting materials, the following compounds are obtained in the same manner as in Reference Example 2.

1-(2-Chloro-4-aminobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, white powder (recrystallized from methanol/diethyl ether), m.p. 194.5 - 195.5°C

1-(3-Methyl-4-aminobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine

^{1}H-NMR ($CDCl_3$) δ : 2.01 (3H, s), 2.41 (3H, s), 2.82-3.21 (3H, m), 3.50-4.21 (4H, m), 4.78-5.14 (1H, m), 6.24-6.40 (1H, m), 6.59-6.82 (2H, m), 6.90-7.18 (3H, m), 7.19-7.34 (1H, m)

5-Dimethylamino-1-(2-chloro-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder (recrystallized from dichloromethane/diethyl ether), m.p. 162 - 164°C

5-Dimethylamino-1-(2-methoxy-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine (recrystallized from methanol/diethyl ether)

^{1}H-NMR ($CDCl_3$) δ : 1.23-2.80 (11H, m), 2.90-3.38 (1H, m), 3.50-5.19 (6H, m), 5.87-6.41 (2H, m), 6.65-7.56 (5H, m)

5-Methoxy-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder (recrystallized from ethyl acetate/n-hexane), m.p. 154 - 155°C

5-Ethoxycarbonylmethoxy-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder (recrystallized from ethyl acetate/n-hexane), m.p. 231 - 232°C

5-(4-Dimethylaminobutoxy)-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless oil

^{1}H-NMR ($CDCl_3$) δ : 1.47-1.83 (6H, m), 1.83-2.54 (4H, m), 2.29 (6H, s), 2.61-3.00 (1H, m), 3.36-3.76 (2H, m), 4.35-5.20 (2H, m), 6.27-6.48 (2H, m), 6.57-6.76 (1H, m), 6.90-7.61 (5H, m)

5-[4-(Phthalimid-1-yl)propoxy]-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless amorphous

^{1}H-NMR ($CDCl_3$) δ : 1.30-2.47 (6H, m), 2.57-3.01 (1H, m), 3.30-4.06 (4H, m), 4.34-5.20 (2H, m), 6.30-6.53

(2H, m), 6.57-6.78 (1H, m), 6.87-7.57 (5H, m), 7.62-7.76 (2H, m), 7.76-7.97 (2H, m)

5-Chloro-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, pale yellow amorphous

^{1}H-NMR ($CDCl_3$) δ : 1.35-4.3 (7H, m), 4.55-6.7 (2H, m), 6.3-6.55 (2H, m), 6.6-6.8 (1H, m), 6.85-7.45 (5H, m)

5-Oxo-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, pale yellow amorphous

^{1}H-NMR ($CDCl_3$) δ : 1.95-2.35 (2H, m), 2.89 (2H, t, J=6.3 Hz), 3.0-5.3 (4H, m), 6.35-6.47 (2H, m), 6.72-6.83 (1H, m), 7.0-7.15 (2H, m), 7.18-7.32 (2H, m), 7.81-7.93 (1H, m)

5-Oxo-1-(2-chloro-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder

^{1}H-NMR ($CDCl_3$) δ : 1.85-2.3 (2H, m), 2.87 (2H, t, J=6.2 Hz), 3.1-4.75 (4H, m), 6.15-7.5 (6H, m), 7.65-7.9 (1H, m)

4-Dimethylaminomethyl-1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline, white powder, m.p. 123 - 125°C

3-Dimethylamino-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 175 - 177°C

3-Dimethylamino-1-(3-methoxy-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, yellow oil

^{1}H-NMR ($CDCl_3$) δ : 1.5-1.7 (1H, m), 2.1-2.3 (1H, m), 2.3-2.6 (1H, m), 2.40 (6H, s), 2.7-3.0 (3H, m), 3.60 (3H, s), 3.8-4.0 (2H, br), 5.2-5.4 (1H, m), 6.37 (1H, d,

J=8.2 Hz), 6.5-6.8 (3H, m), 6.9-7.4 (3H, m)

4-(4-Aminobenzoyl)-3,4-dihydro-2H-1,4-benzothiazine, yellow powder, m.p. 207 - 210°C

5-(4-Aminobenzoyl)-2,3,4,5-tetrahydro-1,5-benzothiazepine, yellow powder, m.p. 193 - 195°C

Reference Example 11

Using the suitable starting materials, the following compounds are obtained in the same manner as in Reference Example 1.

5-Carbamoyloxy-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 243 - 244°C (recrystallized from ethyl acetate/diisopropyl ether)

5-Methylaminocarbonyloxy-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 207 - 208°C (recrystallized from ethyl acetate/n-hexane)

5-Dimethylaminocarbonyloxy-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 155 - 156°C (recrystallized from ethyl acetate/diisopropyl ether/n-hexane)

5-Methylidenyl-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless prisms, m.p. 133.5 - 134°C (recrystallized from ethyl acetate/diisopropyl ether)

5-Oxo-6-methyl-1-(2-chloro-4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless prisms, m.p. 90 - 92°C (recrystallized from ethanol)

1-(4-Nitrobenzoyl)-1,2,3,5-tetrahydro-4,1-

benzothiazepine, yellow powder, m.p. 185 - 187°C (recrystallized from dichloromethane/diethyl ether)

5-Dimethylamino-1-(2-dimethylamino-4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, yellow powder, m.p. 123 - 125°C (recrystallized from diethyl ether/dichloromethane)

5-Oxo-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, white powder, m.p. 201.5 - 202.5°C (recrystallized from diethyl ether/dichloromethane)

5-Oxo-4-methyl-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, white powder, m.p. 136 - 138°C (recrystallized from diethyl ether/dichloromethane)

5-Dimethylamino-1-(3-methyl-4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, yellow oil

^{1}H-NMR ($CDCl_3$) δ : 1.16-3.18 (11H, m), 2.18 (3H, s), 3.40-5.15 (2H, m), 6.50-7.68 (6H, m), 7.70-7.84 (1H, m)

5-Dimethylamino-1-(2-methyl-4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless amorphous

^{1}H-NMR ($CDCl_3$) δ : 1.19-2.86 (11H, m), 2.20 (3H, s), 2.94-3.24 (1H, m), 3.36-5.18 (1H, m), 6.49-8.20 (7H, m)

5-Dimethylamino-1-(2-fluoro-4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, yellow oil

^{1}H-NMR ($CDCl_3$) δ : 1.21-2.66 (10H, m), 2.66-5.11 (3H, m), 6.63-8.25 (7H, m)

5-Dimethylamino-1-(3-fluoro-4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 152 - 152.5°C (recrystallized from chloroform/diethyl ether)

Reference Example 12

Using the suitable starting materials, the following compounds are obtained in the same manner as in Reference Example 2.

5-Carbamoyloxy-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 215 - 216°C (recrystallized from ethyl acetate/n-hexane)

5-Methylaminocarbonyloxy-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 192 - 195°C (recrystallized from ethyl acetate/n-hexane)

5-Dimethylaminocarbonyloxy-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 228 - 230°C (recrystallized from ethyl acetate/diisopropyl ether)

5-Methyl-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 155 - 156°C (recrystallized from ethyl acetate/n-hexane)

5-Oxo-6-methyl-1-(2-chloro-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 193 - 195°C (recrystallized from ethanol)

1-(4-Aminobenzoyl)-1,2,3,5-tetrahydro-4,1-benzothiazepine, white powder, m.p. 179 - 180°C (recrystallized from dichloromethane/diethyl ether)

5-Dimethylamino-1-(2-dimethylamino-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 163 - 165°C (recrystallized from diethyl ether/dichloromethane)

5-Oxo-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-

benzazepine, yellow powder, m.p. 195 - 197°C (recrystallized from diethyl ether/dichloromethane)

5-Oxo-4-methyl-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-1,4-benzazepine, yellow powder, m.p. 190 - 192°C (recrystallized from diethyl ether/dichloromethane)

5-Dimethylamino-1-(2-ethoxy-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 111 - 114°C (recrystallized from diethyl ether)

5-Dimethylamino-1-(3-methyl-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, yellow oil

^{1}H-NMR ($CDCl_3$) δ : 0.66-2.56 (14H, m), 2.93-5.22 (4H, m), 6.23-7.80 (7H, m)

5-Dimethylamino-1-(2-methyl-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 154 - 156°C (recrystallized from methanol/diethyl ether)

5-Dimethylamino-1-(2-fluoro-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 161 - 163°C (recrystallized from dichloromethane/diethyl ether)

5-Dimethylamino-1-(3-fluoro-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 156 - 157°C (recrystallized from methanol/diethyl ether)

5-Oxo-1-(2-methoxy-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless prisms, m.p. 160 - 160.5°C (recrystallized from methanol/diethyl ether)

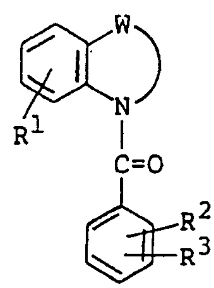
Example 1

To a solution of 1,2,3,4-tetrahydroquinoline (28.7

g) in acetone (400 ml) and water (200 ml) is added potassium carbonate (38.8 g) and further thereto is added 4-benzoylaminobenzoyl chloride (56 g) under ice-cooling. The mixture is stirred at room temperature overnight. Water is added to the reaction mixture, and the mixture is extracted with dichloromethane. The extract is dried over magnesium sulfate, and the solvent is distilled off under reduced pressure. The resulting residue is purified by silica gel column chromatography and recrystallized from methanol to give 1-[4-(benzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (57 g) as white powder, m.p. 202.5 - 203.5°C.

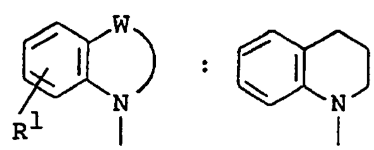
Using the suitable starting materials, the compounds as shown in the following Table 1 are obtained in the same manner as in Example 1.

Table 1

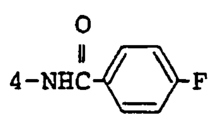


Example 2

Structure



R^2: H

R^3: 

Crystalline form: Light yellow powder

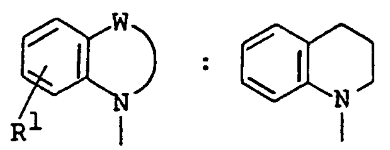
Recrystallization solvent: Methanol

Melting Point: 198.5 - 199.5°C

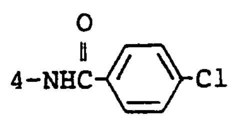
Form: Free

Example 3

Structure



R^2: H

R^3: 

Crystalline form: White powder

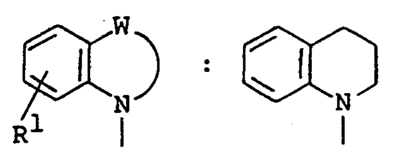
Recrystallization solvent: Methanol

Melting Point: 200.5 - 201.5°C

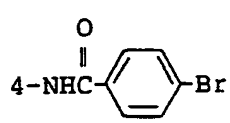
Form: Free

Example 4

Structure



R^2: H

R^3: 

Crystalline form: Yellow powder

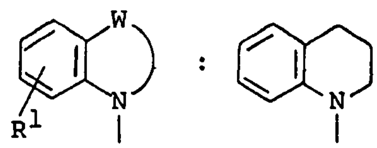
Recrystallization solvent: Methanol

Melting Point: 206 - 207°C

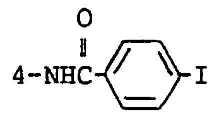
Form: Free

Example 5

Structure



R^2: H

R^3: 

Crystalline form: Yellow powder

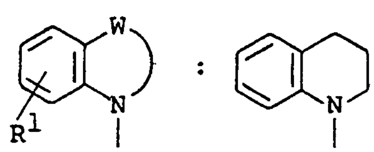
Recrystallization solvent: Methanol

Melting Point: 216 - 217°C

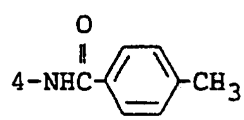
Form: Free

Example 6

Structure



R^2: H

R^3: 

Crystalline form: White powder

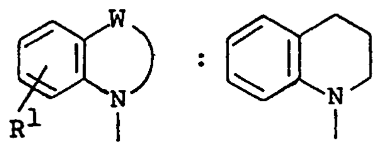
Recrystallization solvent: Methanol

Melting Point: 202 - 203°C

Form: Free

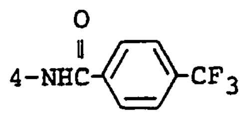
Example 7

Structure



R^2: H

R^3:



Crystalline form: White powder

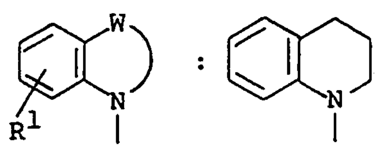
Recrystallization solvent: Methanol

Melting Point: 212 - 213°C

Form: Free

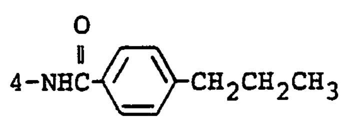
Example 8

Structure



R^2: H

R^3:



Crystalline form: White powder

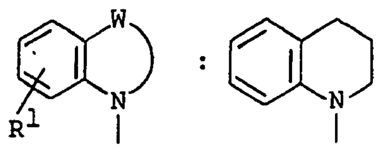
Recrystallization solvent: Methanol

Melting Point: 167.5 - 168.5°C

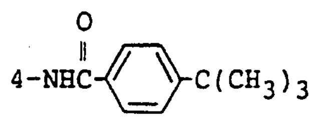
Form: Free

Example 9

Structure



R^2: H

R^3: 

Crystalline form: White powder

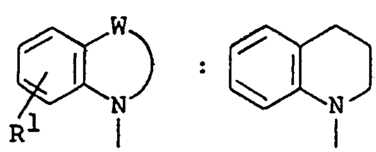
Recrystallization solvent: Methanol

Melting Point: 205 - 206°C

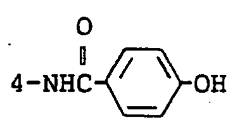
Form: Free

Example 10

Structure



R^2: H

R^3: 

Crystalline form: White powder

Recrystallization solvent: Methanol

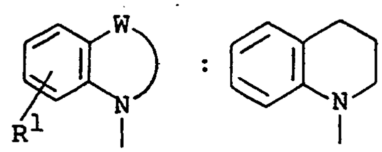
Melting Point: >300°C

NMR analysis: 1)

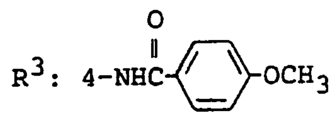
Form: Free

Example 11

Structure



R^2: H



Crystalline form: Yellow powder

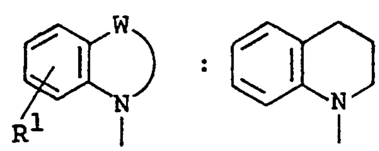
Recrystallization solvent: Methanol

Melting Point: 176 - 177°C

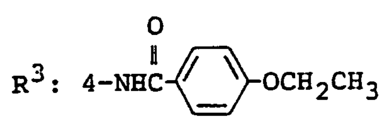
Form: Free

Example 12

Structure



R^2: H



Crystalline form: White powder

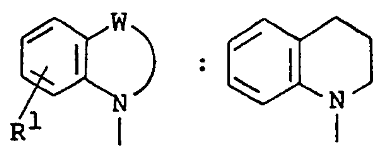
Recrystallization solvent: Methanol

Melting Point: 219 - 220°C

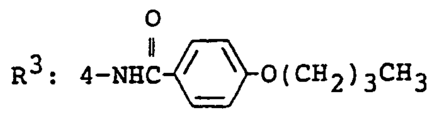
Form: Free

Example 13

Structure



R^2: H



Crystalline form: White powder

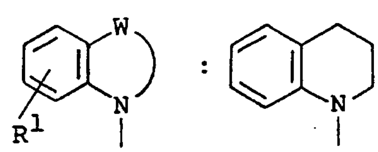
Recrystallization solvent: Methanol

Melting Point: 193 - 194°C

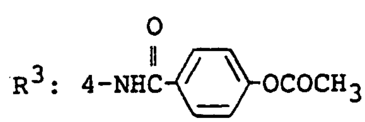
Form: Free

Example 14

Structure



R^2: H



Crystalline form: White powder

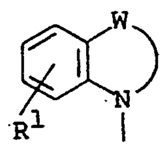
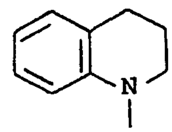
Recrystallization solvent: Methanol

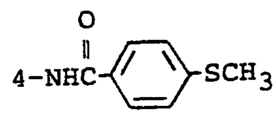
Melting Point: 232 - 233°C

Form: Free

Example 15

Structure

 :  R^2: H

R^3: 

Crystalline form: White powder

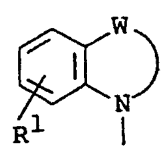
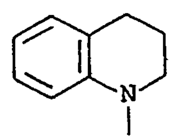
Recrystallization solvent: Methanol

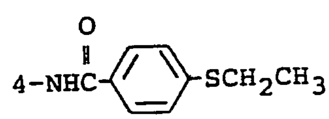
Melting Point: 209 - 210°C

Form: Free

Example 16

Structure

 :  R^2: H

R^3: 

Crystalline form: White powder

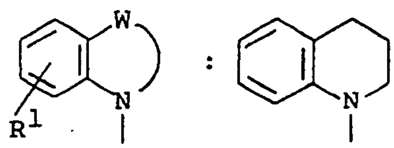
Recrystallization solvent: Methanol

Melting Point: 184.5 - 185.5°C

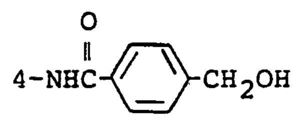
Form: Free

Example 17

Structure



R^2: H

R^3: 

Crystalline form: White powder

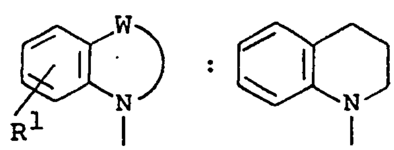
Recrystallization solvent: Methanol

Melting Point: 224.5 - 225.5°C

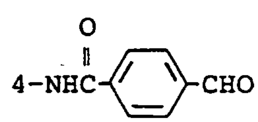
Form: Free

Example 18

Structure



R^2: H

R^3: 

Crystalline form: White powder

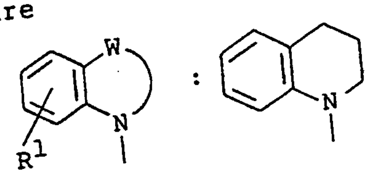
Recrystallization solvent: Methanol

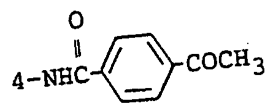
Melting Point: 220.5 - 221.5°C

Form: Free

Example 19

Structure



R^3: 

Crystalline form: Yellow powder

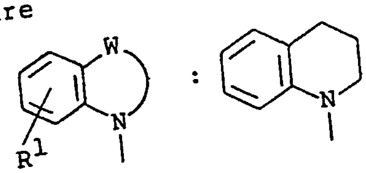
Recrystallization solvent: Methanol

Melting Point: 231 - 232°C

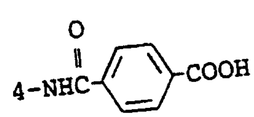
Form: Free

Example 20

Structure



R^2: H

R^3: 

Crystalline form: White powder

Recrystallization solvent: Methanol

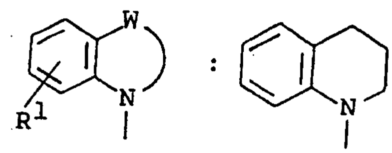
Melting Point: >300°C

NMR analysis: 2)

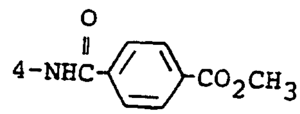
Form: Free

Example 21

Structure



R^2: H

R^3: 

Crystalline form: White powder

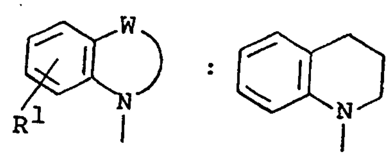
Recrystallization solvent: Methanol

Melting Point: 208 - 209°C

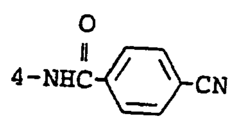
Form: Free

Example 22

Structure



R^2: H

R^3: 

Crystalline form: White powder

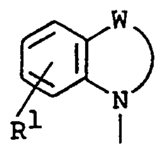
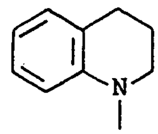
Recrystallization solvent: Methanol

Melting Point: 234.5 - 235.5°C

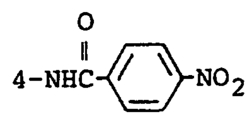
Form: Free

Example 23

Structure

 : 

R^2: H

R^3: 

Crystalline form: Yellow powder

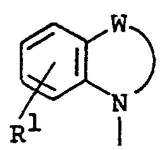
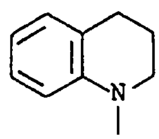
Recrystallization solvent: Methanol

Melting Point: 263.5 - 264.5°C

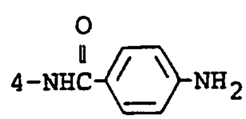
Form: Free

Example 24

Structure

 : 

R^2: H

R^3: 

Crystalline form: White powder

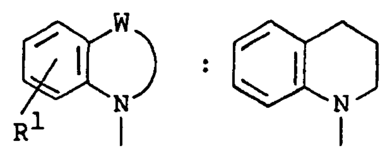
Recrystallization solvent: Methanol

Melting Point: 237 - 238°C

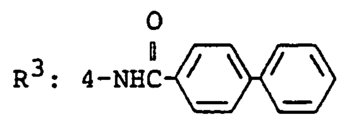
Form: Free

Example 25

Structure



R^2: H



Crystalline form: White powder

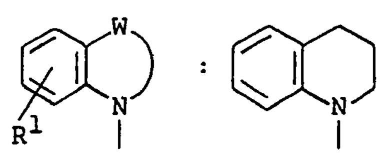
Recrystallization solvent: Methanol

Melting Point: 234 - 235°C

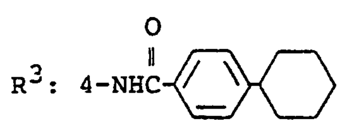
Form: Free

Example 26

Structure



R^2: H



Crystalline form: White powder

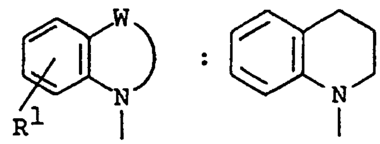
Recrystallization solvent: Methanol

Melting Point: 236.5 - 237.5°C

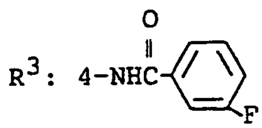
Form: Free

Example 27

Structure



R^2: H



Crystalline form: White powder

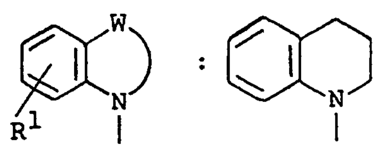
Recrystallization solvent: Methanol

Melting Point: 206.5 - 207.5°C

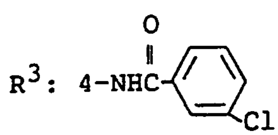
Form: Free

Example 28

Structure



R^2: H



Crystalline form: White powder

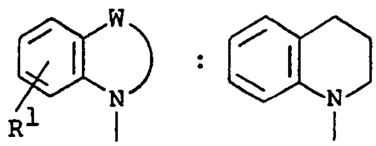
Recrystallization solvent: Methanol

Melting Point: 210 - 211°C

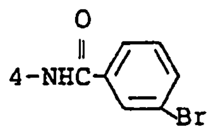
Form: Free

Example 29

Structure



R^2: H

R^3: 

Crystalline form: White powder

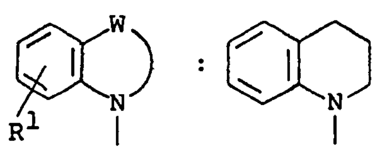
Recrystallization solvent: Methanol

Melting Point: 210.5 - 211.5°C

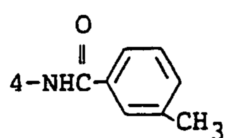
Form: Free

Example 30

Structure



R^2: H

R^3: 

Crystalline form: White powder

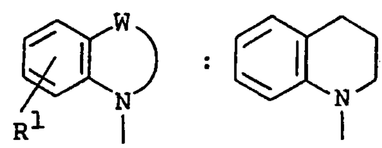
Recrystallization solvent: Methanol

Melting Point: 178 - 179°C

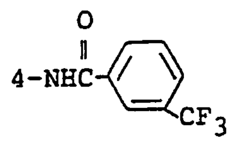
Form: Free

Example 31

Structure



R^2: H

R^3: 

Crystalline form: White powder

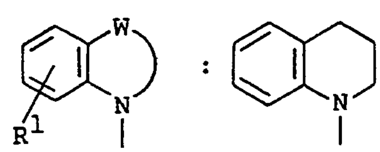
Recrystallization solvent: Methanol

Melting Point: 192 - 193°C

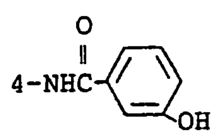
Form: Free

Example 32

Structure



R^2: H

R^3: 

Crystalline form: White powder

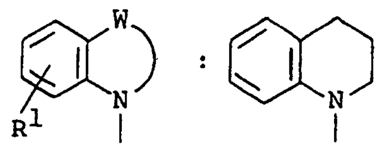
Recrystallization solvent: Methanol

Melting Point: 217 - 218°C

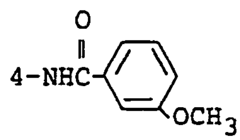
Form: Free

Example 33

Structure



R^2: H

R^3: 

Crystalline form: White powder

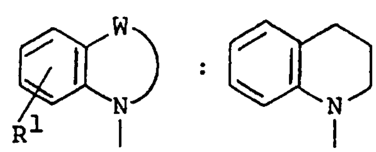
Recrystallization solvent: Methanol

Melting Point: 143 - 144°C

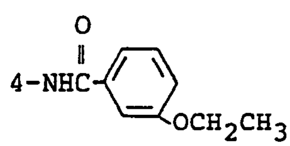
Form: Free

Example 34

Structure



R^2: H

R^3: 

Crystalline form: White powder

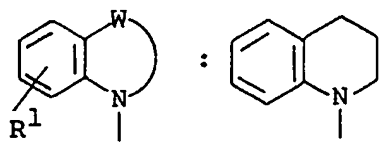
Recrystallization solvent: Methanol

Melting Point: 170.5 - 171.5°C

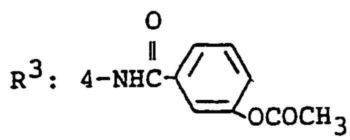
Form: Free

Example 35

Structure



R^2: H



Crystalline form: White powder

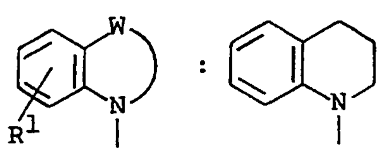
Recrystallization solvent: Methanol

Melting Point: 169.5 - 170.5°C

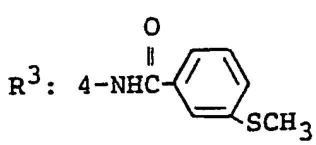
Form: Free

Example 36

Structure



R^2: H



Crystalline form: White powder

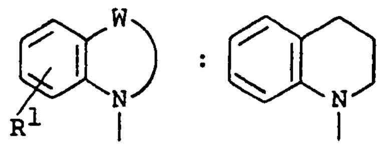
Recrystallization solvent: Methanol

Melting Point: 174.5 - 175.5°C

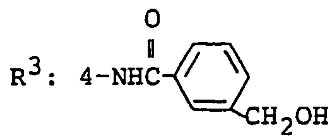
Form: Free

Example 37

Structure



R^2: H



Crystalline form: White powder

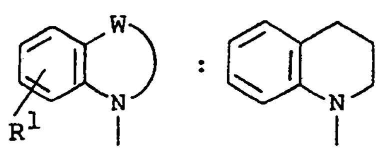
Recrystallization solvent: Methanol

Melting Point: 148.5 - 149.5°C

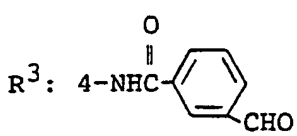
Form: Free

Example 38

Structure



R^2: H



Crystalline form: White powder

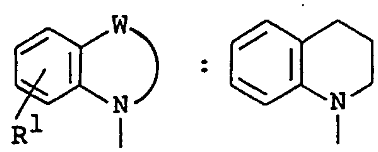
Recrystallization solvent: Methanol

Melting Point: 165 - 166°C

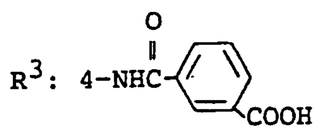
Form: Free

Example 39

Structure



R^2: H



Crystalline form: White powder

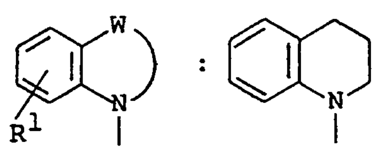
Recrystallization solvent: Methanol

Melting Point: 243 - 244°C

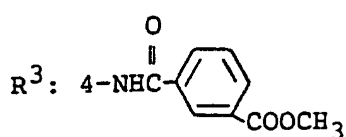
Form: Free

Example 40

Structure



R^2: H



Crystalline form: White powder

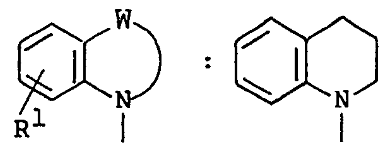
Recrystallization solvent: Methanol

Melting Point: 199 - 200°C

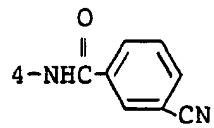
Form: Free

Example 41

Structure



R^2: H

R^3: 

Crystalline form: White powder

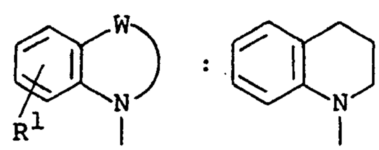
Recrystallization solvent: Methanol

Melting Point: 232.5 - 233.5°C

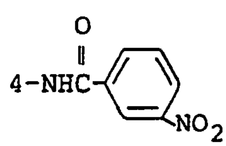
Form: Free

Example 42

Structure



R^2: H

R^3: 

Crystalline form: White powder

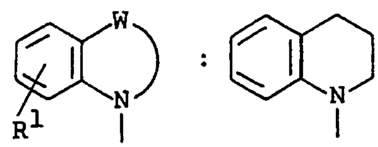
Recrystallization solvent: Methanol

Melting Point: 178.5 - 179.5°C

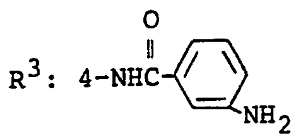
Form: Free

Example 43

Structure



R^2: H



Crystalline form: White powder

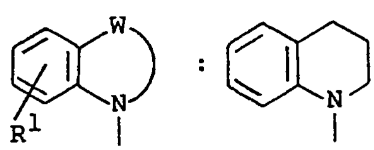
Recrystallization solvent: Methanol

Melting Point: 205.5 - 206.5°C

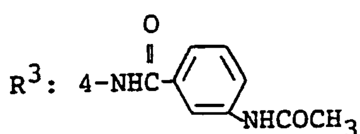
Form: Free

Example 44

Structure



R^2: H



Crystalline form: White powder

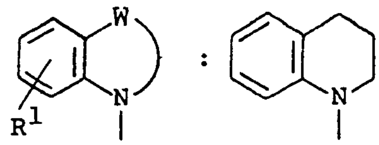
Recrystallization solvent: Methanol

Melting Point: 234 - 235°C

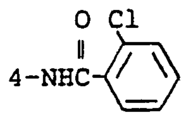
Form: Free

Example 45

Structure



R^2: H

R^3: 

Crystalline form: White powder

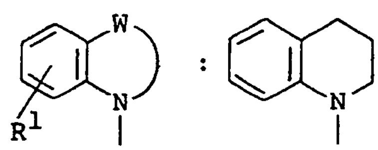
Recrystallization solvent: Methanol

Melting Point: 225 - 226°C

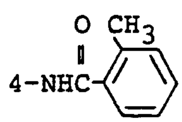
Form: Free

Example 46

Structure



R^2: H

R^3: 

Crystalline form: White powder

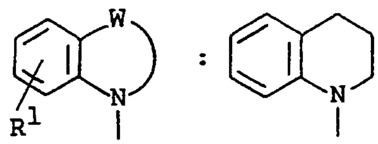
Recrystallization solvent: Methanol

Melting Point: 224 - 225°C

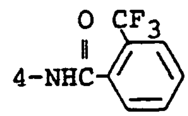
Form: Free

Example 47

Structure



R^2: H

R^3: 

Crystalline form: White powder

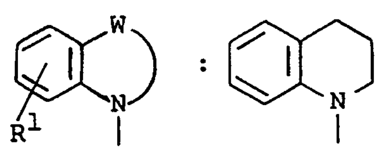
Recrystallization solvent: Methanol

Melting Point: 236 - 237°C

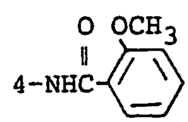
Form: Free

Example 48

Structure



R^2: H

R^3: 

Crystalline form: Yellow powder

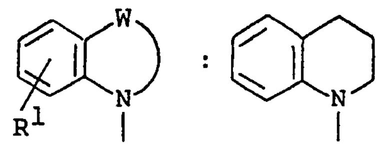
Recrystallization solvent: Methanol

Melting Point: 175.5 - 176.5°C

Form: Free

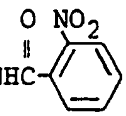
Example 49

Structure



R^2: H

R^3: 4-NHC-



Crystalline form: White powder

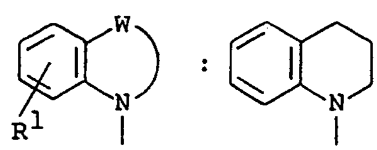
Recrystallization solvent: Methanol

Melting Point: 231 - 232°C

Form: Free

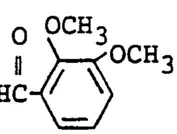
Example 50

Structure



R^2: H

R^3: 4-NHC-



Crystalline form: Yellow powder

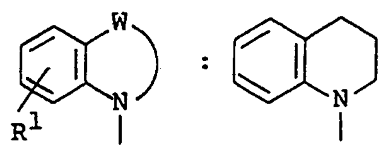
Recrystallization solvent: Methanol

Melting Point: 204 - 205°C

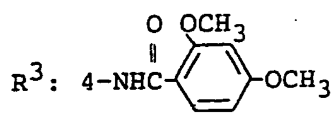
Form: Free

Example 51

Structure



R^2: H



Crystalline form: White powder

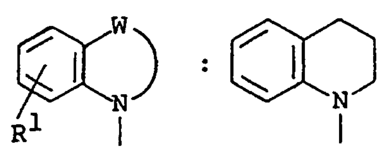
Recrystallization solvent: Methanol

Melting Point: 190 - 191°C

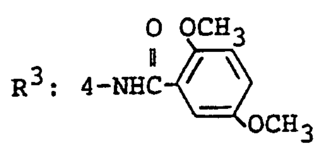
Form: Free

Example 52

Structure



R^2: H



Crystalline form: White powder

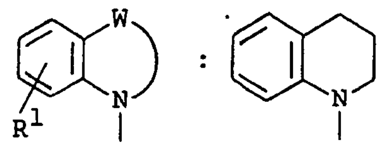
Recrystallization solvent: Methanol

Melting Point: 156 - 157°C

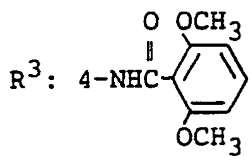
Form: Free

Example 53

Structure



R^2: H



Crystalline form: White powder

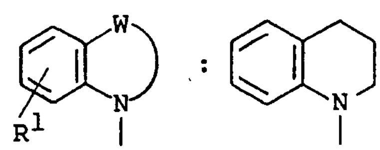
Recrystallization solvent: Methanol

Melting Point: 200 - 201°C

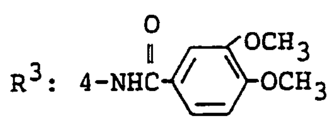
Form: Free

Example 54

Structure



R^2: H



Crystalline form: White powder

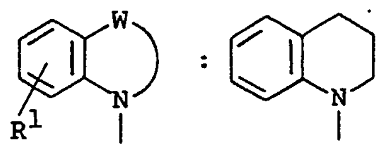
Recrystallization solvent: Methanol

Melting Point: 206 - 207°C

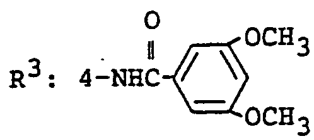
Form: Free

Example 55

Structure



R^2: H



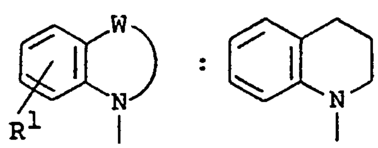
Crystalline form: Colorless amorphous

NMR analysis: 3)

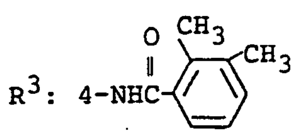
Form: Free

Example 56

Structure



R^2: H



Crystalline form: White powder

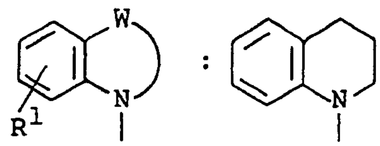
Recrystallization solvent: Methanol

Melting Point: 215.5 - 216.5°C

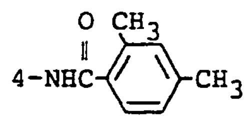
Form: Free

Example 57

Structure



R^2: H

R^3: 

Crystalline form: White powder

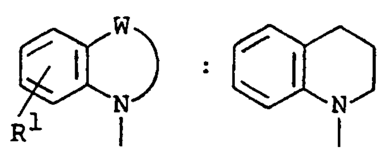
Recrystallization solvent: Methanol

Melting Point: 189 - 190°C

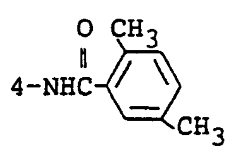
Form: Free

Example 58

Structure



R^2: H

R^3: 

Crystalline form: White powder

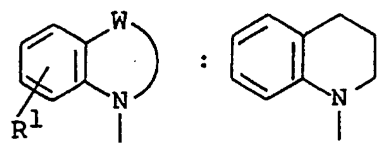
Recrystallization solvent: Methanol

Melting Point: 203.5 - 204.5°C

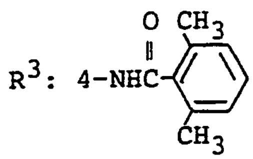
Form: Free

Example 59

Structure



R^2: H



Crystalline form: Yellow powder

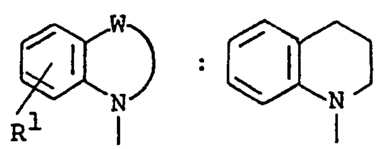
Recrystallization solvent: Methanol

Melting Point: 254.5 - 255.5°C

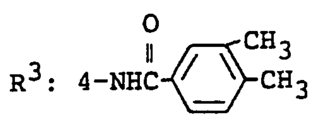
Form: Free

Example 60

Structure



R^2: H



Crystalline form: Brown powder

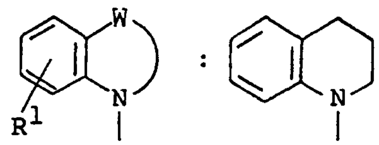
Recrystallization solvent: Methanol

Melting Point: 182.5 - 183.5°C

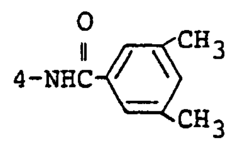
Form: Free

Example 61

Structure



R^2: H

R^3: 

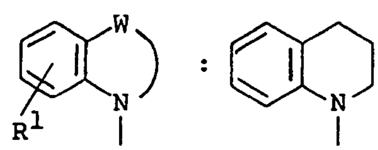
Crystalline form: Colorless amorphous

NMR analysis: 4)

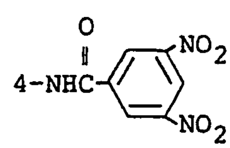
Form: Free

Example 62

Structure



R^2: H

R^3: 

Crystalline form: White powder

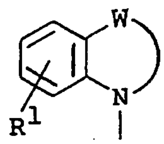
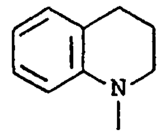
Recrystallization solvent: Methanol

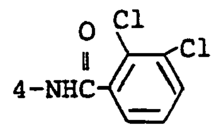
Melting Point: 263 - 264°C

Form: Free

Example 63

Structure

 :  R^2: H

R^3: 

Crystalline form: White powder

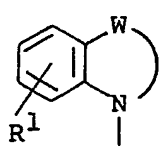
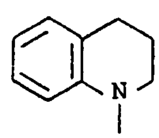
Recrystallization solvent: Dichloromethane/ethanol

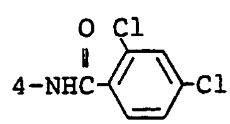
Melting Point: 217 - 218°C

Form: Free

Example 64

Structure

 :  R^2: H

R^3: 

Crystalline form: White powder

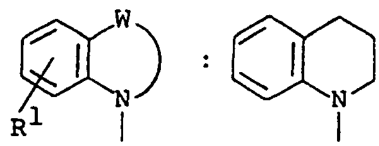
Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 183 - 184°C

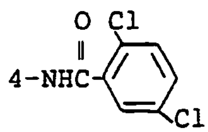
Form: Free

Example 65

Structure



R^2: H

R^3: 

Crystalline form: Yellow powder

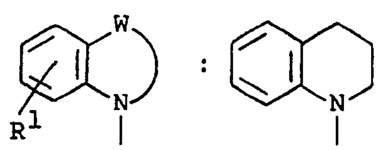
Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 207.5 - 208.5°C

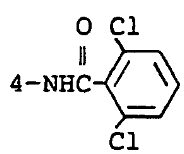
Form: Free

Example 66

Structure



R^2: H

R^3: 

Crystalline form: Yellow powder

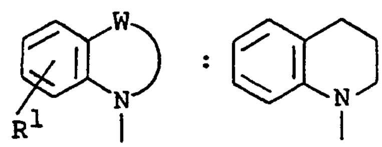
Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 251 - 252°C

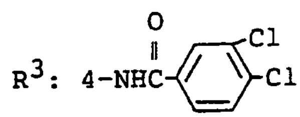
Form: Free

Example 67

Structure



R^2: H



Crystalline form: White powder

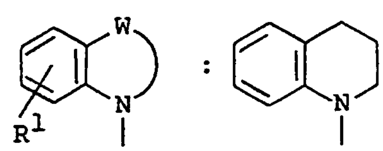
Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 208.5 - 209.5°C

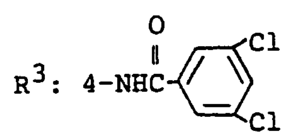
Form: Free

Example 68

Structure



R^2: H



Crystalline form: White powder

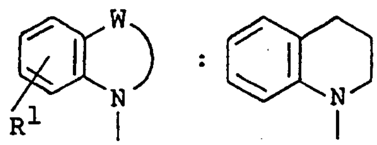
Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 231 - 232°C

Form: Free

Example 69

Structure



R^2: H

R^3: 4-NHC(=O)CH_3

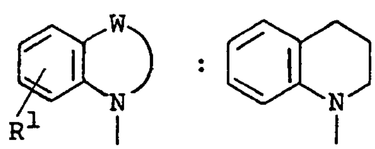
Crystalline form: Colorless amorphous

NMR analysis: 5)

Form: Free

Example 70

Structure



R^2: H

R^3: 4-NHC(=O)$(CH_2)_2CH_3$

Crystalline form: White powder

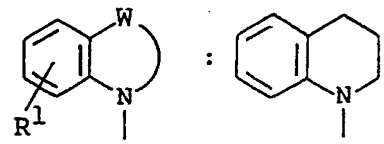
Recrystallization solvent: Methanol

Melting Point: 134 - 135°C

Form: Free

Example 71

Structure



R^2: H

R^3: 4-NHC(O)$(CH_2)_4CH_3$

Crystalline form: Yellow powder

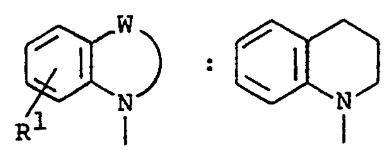
Recrystallization solvent: Methanol

Melting Point: 115 - 116°C

Form: Free

Example 72

Structure



R^2: H

R^3: 4-NHC(O)$CH_2C(CH_3)_3$

Crystalline form: White powder

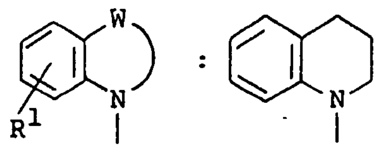
Recrystallization solvent: Methanol

Melting Point: 178.5 - 179.5°C

Form: Free

Example 73

Structure



R^2: H

R^3: 4-$NHC(=O)CH(CH_3)_2$

Crystalline form: White powder

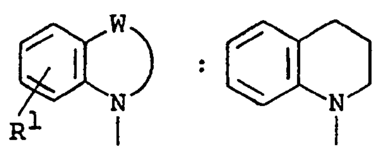
Recrystallization solvent: Methanol

Melting Point: 182.5 - 183.5°C

Form: Free

Example 74

Structure



R^2: H

R^3: 4-$NHC(=O)C(CH_3)_3$

Crystalline form: White powder

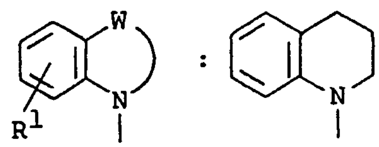
Recrystallization solvent: Methanol

Melting Point: 164 - 165°C

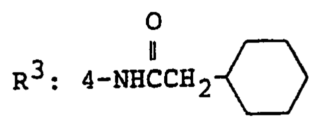
Form: Free

Example 75

Structure



R^2: H



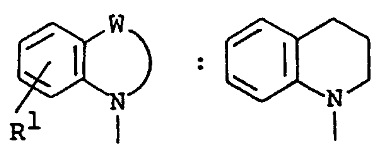
Crystalline form: Colorless amorphous

NMR analysis: 6)

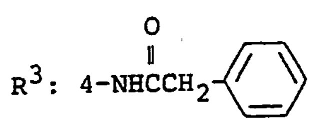
Form: Free

Example 76

Structure



R^2: H



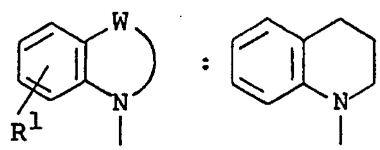
Crystalline form: Yellow amorphous

NMR analysis: 7)

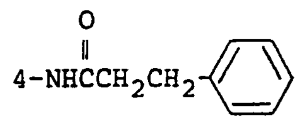
Form: Free

Example 77

Structure



R^2: H

R^3: 

Crystalline form: White powder

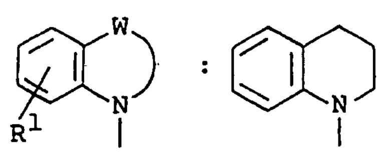
Recrystallization solvent: Methanol

Melting Point: 155 - 156°C

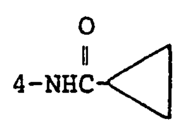
Form: Free

Example 78

Structure



R^2: H

R^3: 

Crystalline form: White powder

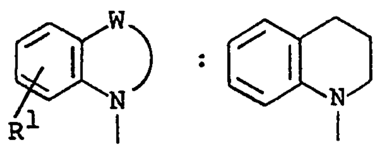
Recrystallization solvent: Methanol

Melting Point: 182.5 - 183.5°C

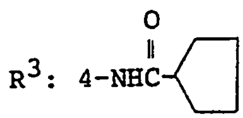
Form: Free

Example 79

Structure



R^2: H



Crystalline form: White powder

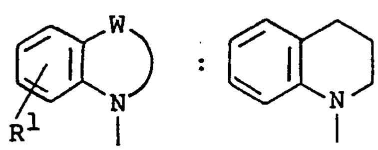
Recrystallization solvent: Methanol

Melting Point: 164.5 - 165.5°C

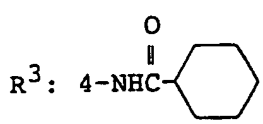
Form: Free

Example 80

Structure



R^2: H



Crystalline form: White powder

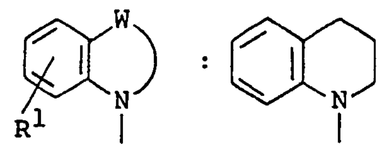
Recrystallization solvent: Methanol

Melting Point: 165 - 167°C

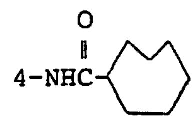
Form: Free

Example 81

Structure



R^2: H

R^3: 

Crystalline form: White powder

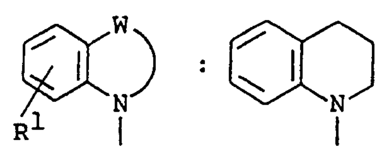
Recrystallization solvent: Methanol

Melting Point: 124 - 125°C

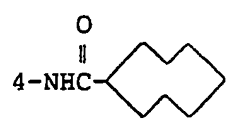
Form: Free

Example 82

Structure



R^2: H

R^3: 

Crystalline form: White powder

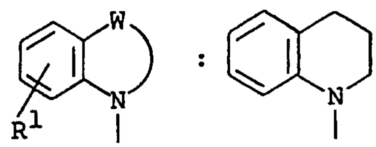
Recrystallization solvent: Methanol

Melting Point: 140.5 - 141.5°C

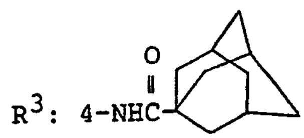
Form: Free

Example 83

Structure



R^2: H



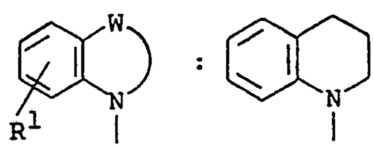
Crystalline form: Colorless amorphous

NMR analysis: 8)

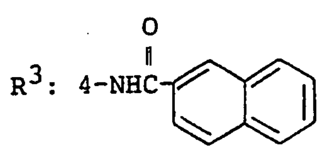
Form: Free

Example 84

Structure



R^2: H



Crystalline form: White powder

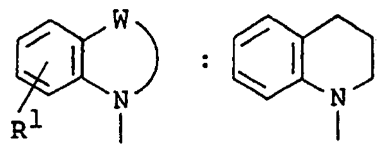
Recrystallization solvent: Methanol

Melting Point: 211 - 212°C

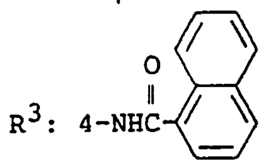
Form: Free

Example 85

Structure



R^2: H



Crystalline form: White powder

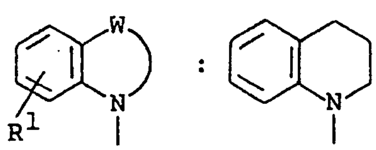
Recrystallization solvent: Methanol

Melting Point: 178 - 179°C

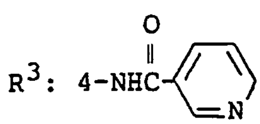
Form: Free

Example 86

Structure



R^2: H



Crystalline form: White powder

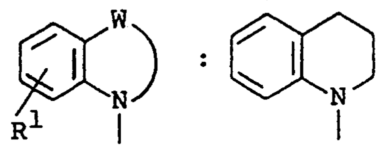
Recrystallization solvent: Methanol

Melting Point: 212.5 - 213.5°C

Form: Free

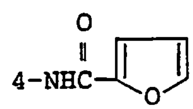
Example 87

Structure



R^2: H

R^3:



Crystalline form: White powder

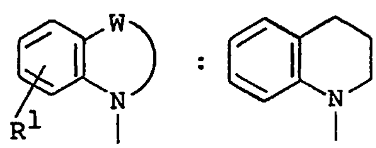
Recrystallization solvent: Methanol

Melting Point: 193 - 194°C

Form: Free

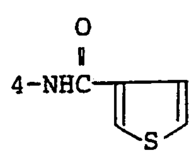
Example 88

Structure



R^2: H

R^3:



Crystalline form: White powder

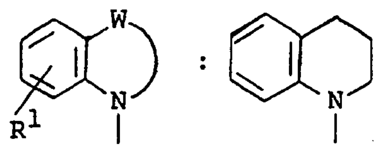
Recrystallization solvent: Methanol

Melting Point: 203 - 204°C

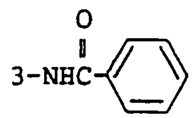
Form: Free

Example 89

Structure



R^2: H

R^3: 

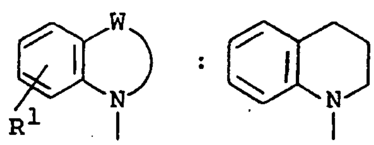
Crystalline form: Colorless amorphous

NMR analysis: 9)

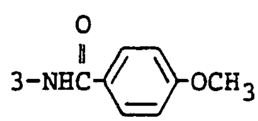
Form: Free

Example 90

Structure



R^2: H

R^3: 

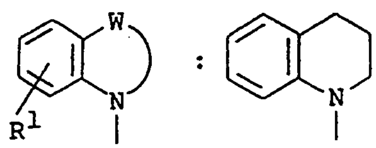
Crystalline form: Colorless amorphous

NMR analysis: 10)

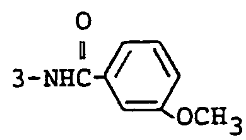
Form: Free

Example 91

Structure



R^2: H

R^3: 

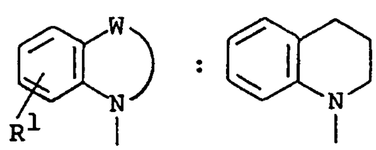
Crystalline form: Colorless amorphous

NMR analysis: 11)

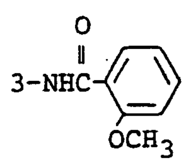
Form: Free

Example 92

Structure



R^2: H

R^3: 

Crystalline form: White powder

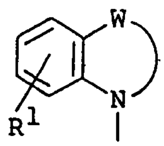
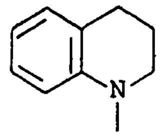
Recrystallization solvent: Methanol

Melting Point: 156.5 - 157.5°C

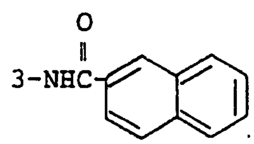
Form: Free

Example 93

Structure

 : 

R^2: H

R^3: 

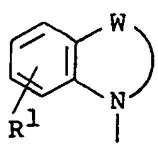
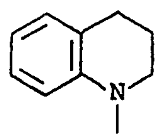
Crystalline form: Colorless amorphous

NMR analysis: 12)

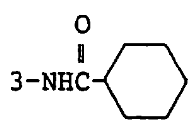
Form: Free

Example 94

Structure

 : 

R^2: H

R^3: 

Crystalline form: White powder

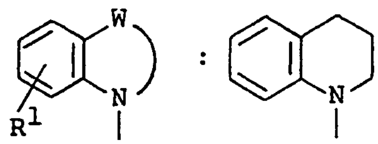
Recrystallization solvent: Methanol

Melting Point: 203.5 - 204.5°C

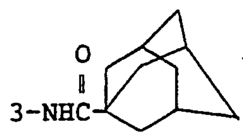
Form: Free

Example 95

Structure



R^2: H

R^3:


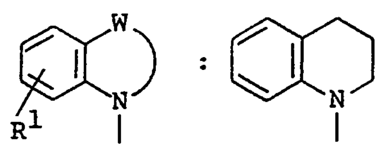
Crystalline form: Colorless amorphous

NMR analysis: 13)

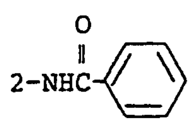
Form: Free

Example 96

Structure



R^2: H

R^3:


Crystalline form: Yellow powder

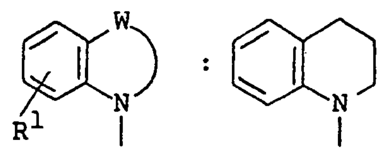
Recrystallization solvent: Methanol

Melting Point: 126 - 127°C

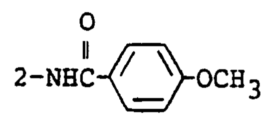
Form: Free

Example 97

Structure



R^2: H

R^3: 

Crystalline form: White powder

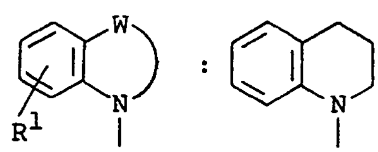
Recrystallization solvent: Methanol

Melting Point: 158.5 - 159.5°C

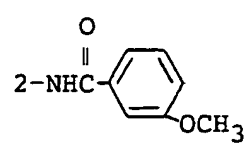
Form: Free

Example 98

Structure



R^2: H

R^3: 

Crystalline form: White powder

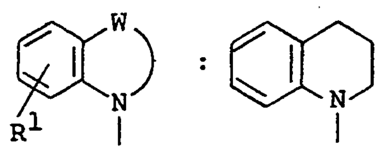
Recrystallization solvent: Methanol

Melting Point: 129 - 130°C

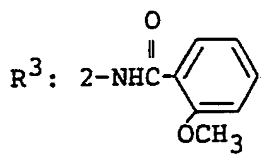
Form: Free

Example 99

Structure



R^2: H



Crystalline form: White powder

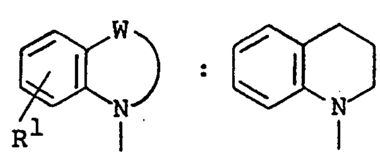
Recrystallization solvent: Methanol

Melting Point: 131.5 - 132.5°C

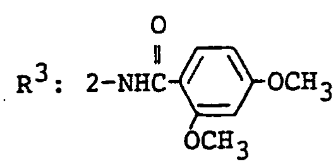
Form: Free

Example 100

Structure



R^2: H



Crystalline form: White powder

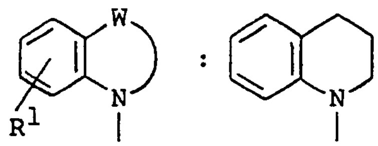
Recrystallization solvent: Methanol

Melting Point: 140 - 141°C

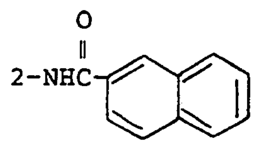
Form: Free

Example 101

Structure



R^2: H

R^3: 

Crystalline form: White powder

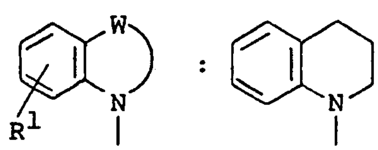
Recrystallization solvent: Methanol

Melting Point: 138.5 - 139.5°C

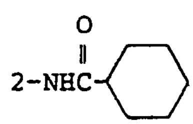
Form: Free

Example 102

Structure



R^2: H

R^3: 

Crystalline form: White powder

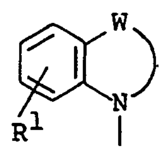
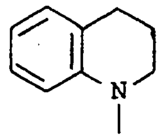
Recrystallization solvent: Methanol

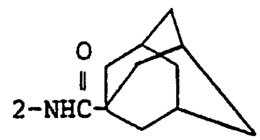
Melting Point: 128 - 129°C

Form: Free

Example 103

Structure

 :  R^2: H

R^3: 

Crystalline form: White powder

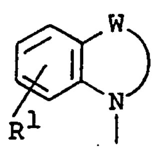
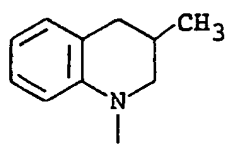
Recrystallization solvent: Methanol

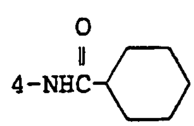
Melting Point: 160 - 161°C

Form: Free

Example 104

Structure

 :  R^2: H

R^3: 

Crystalline form: White powder

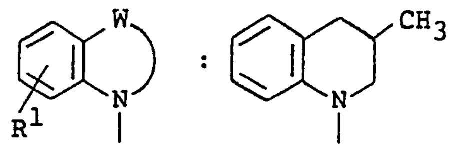
Recrystallization solvent: Methanol

Melting Point: 175 - 176°C

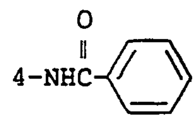
Form: Free

Example 105

Structure



R^2: H

R^3: 

Crystalline form: White powder

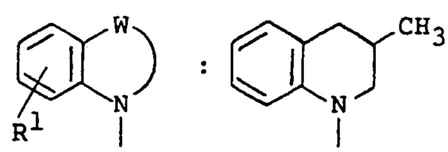
Recrystallization solvent: Methanol

Melting Point: 197 - 198°C

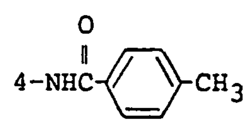
Form: Free

Example 106

Structure



R^2: H

R^3: 

Crystalline form: White powder

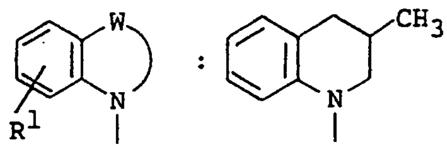
Recrystallization solvent: Methanol

Melting Point: 204 - 205°C

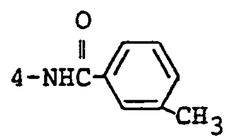
Form: Free

Example 107

Structure



R^2: H

R^3: 

Crystalline form: White powder

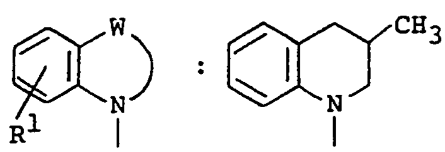
Recrystallization solvent: Methanol

Melting Point: 174 - 175°C

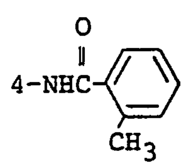
Form: Free

Example 108

Structure



R^2: H

R^3: 

Crystalline form: Yellow powder

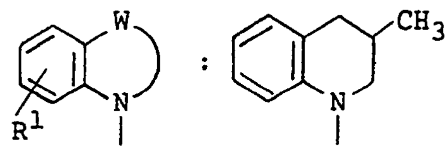
Recrystallization solvent: Methanol

Melting Point: 202 - 203°C

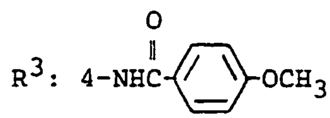
Form: Free

Example 109

Structure



R^2: H



Crystalline form: White powder

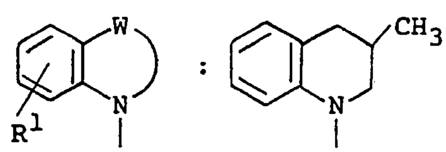
Recrystallization solvent: Methanol

Melting Point: 203 - 204°C

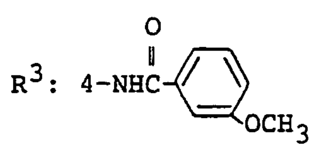
Form: Free

Example 110

Structure



R^2: H



Crystalline form: White powder

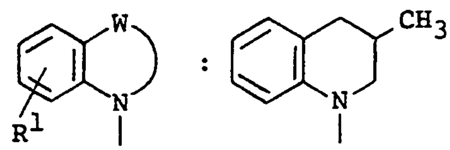
Recrystallization solvent: Methanol

Melting Point: 170.5 - 171.5°C

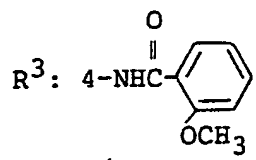
Form: Free

Example 111

Structure



R^2: H



Crystalline form: White powder

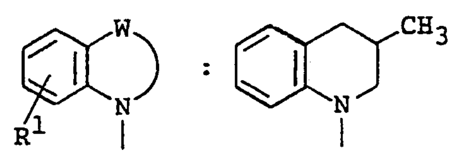
Recrystallization solvent: Methanol

Melting Point: 149 - 150°C

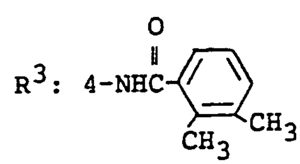
Form: Free

Example 112

Structure



R^2: H



Crystalline form: White powder

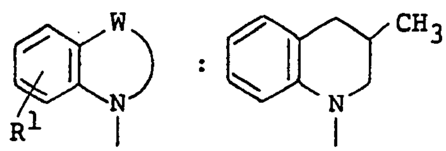
Recrystallization solvent: Methanol

Melting Point: 185 - 186°C

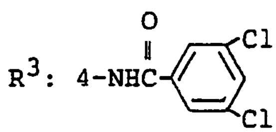
Form: Free

Example 113

Structure



R^2: H



Crystalline form: White powder

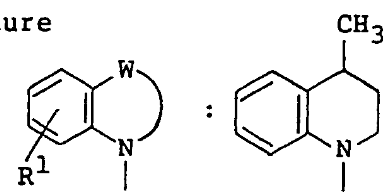
Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 225 - 226°C

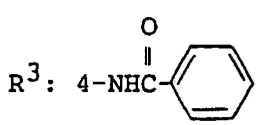
Form: Free

Example 114

Structure



R^2: H



Crystalline form: White powder

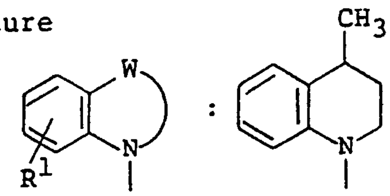
Recrystallization solvent: Methanol

Melting Point: 234 - 235°C

Form: Free

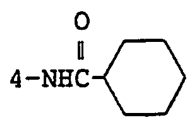
Example 115

Structure



R^2: H

R^3:



Crystalline form: White powder

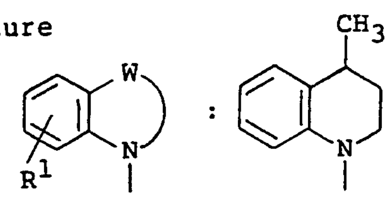
Recrystallization solvent: Methanol

Melting Point: 149.5 - 150.5°C

Form: Free

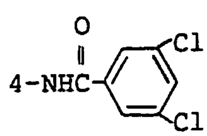
Example 116

Structure



R^2: H

R^3:



Crystalline form: White powder

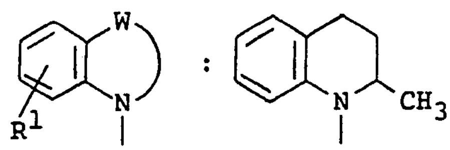
Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 197 - 198°C

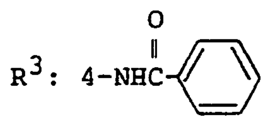
Form: Free

Example 117

Structure



R^2: H



Crystalline form: White powder

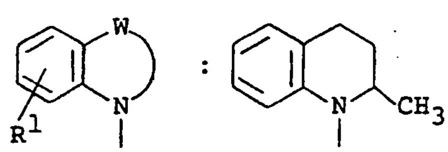
Recrystallization solvent: Methanol

Melting Point: 204 - 205°C

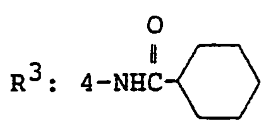
Form: Free

Example 118

Structure



R^2: H



Crystalline form: White powder

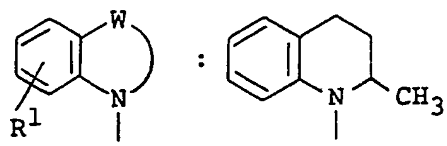
Recrystallization solvent: Methanol

Melting Point: 224.5 - 225.5°C

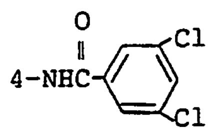
Form: Free

Example 119

Structure



R^2: H

R^3: 

Crystalline form: White powder

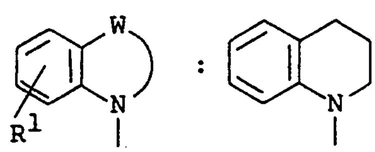
Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 189.5 - 190.5°C

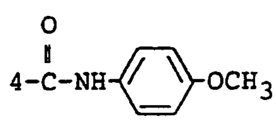
Form: Free

Example 120

Structure



R^2: H

R^3: 

Crystalline form: White powder

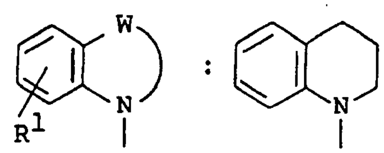
Recrystallization solvent: Methanol

Melting Point: 221.5 - 222.5°C

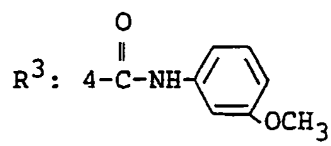
Form: Free

Example 121

Structure



R^2: H



Crystalline form: Colorless needles

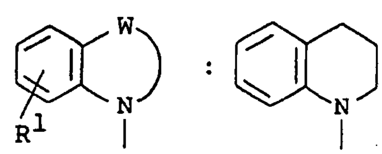
Recrystallization solvent: Methanol

Melting Point: 154 - 155°C

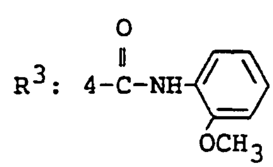
Form: Free

Example 122

Structure



R^2: H



Crystalline form: White powder

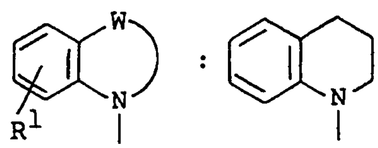
Recrystallization solvent: Methanol

Melting Point: 165 - 166°C

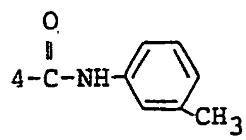
Form: Free

Example 123

Structure



R^2: H

R^3: 

Crystalline form: Colorless needles

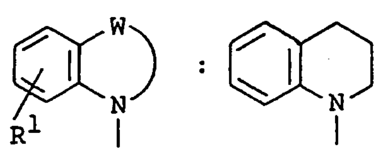
Recrystallization solvent: Methanol

Melting Point: 141 - 142°C

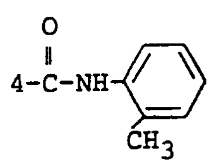
Form: Free

Example 124

Structure



R^2: H

R^3: 

Crystalline form: White powder

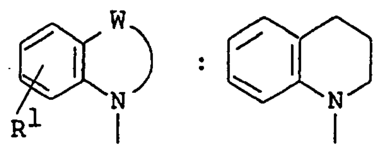
Recrystallization solvent: Methanol

Melting Point: 165.5 - 166.5°C

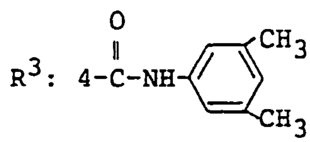
Form: Free

Example 125

Structure



R^2: H



Crystalline form: Colorless needles

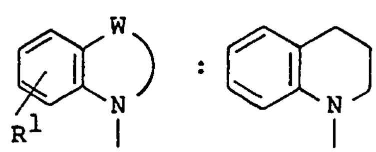
Recrystallization solvent: Methanol

Melting Point: 164 - 165°C

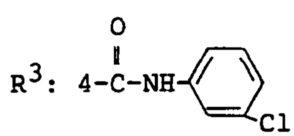
Form: Free

Example 126

Structure



R^2: H



Crystalline form: White powder

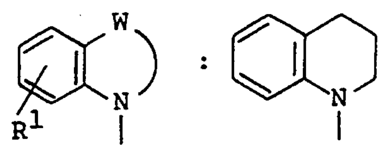
Recrystallization solvent: Methanol

Melting Point: 203.5 - 204.5°C

Form: Free

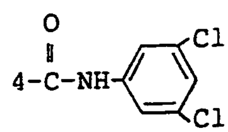
Example 127

Structure



R^2: H

R^3:



Crystalline form: White powder

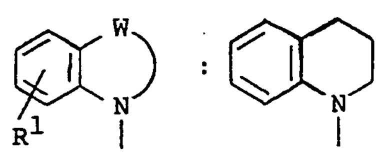
Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 236.5 - 237.5°C

Form: Free

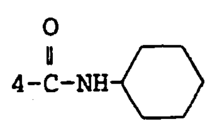
Example 128

Structure



R^2: H

R^3:



Crystalline form: White powder

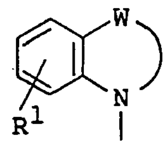
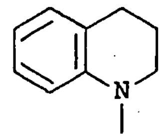
Recrystallization solvent: Methanol

Melting Point: 206.5 - 207.5°C

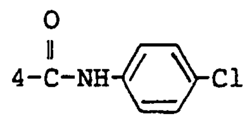
Form: Free

Example 129

Structure

 : 

R^2: H

R^3: 

Crystalline form: White powder

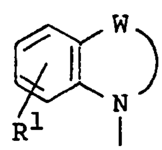
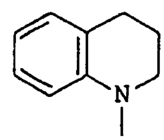
Recrystallization solvent: Methanol

Melting Point: 271 - 272°C

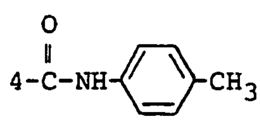
Form: Free

Example 130

Structure

 : 

R^2: H

R^3: 

Crystalline form: White powder

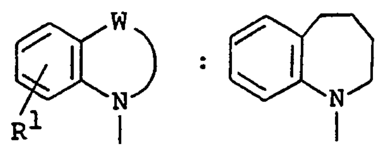
Recrystallization solvent: Methanol

Melting Point: 246 - 247°C

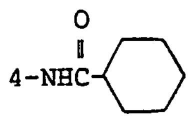
Form: Free

Example 131

Structure



R^2: H

R^3: 

Crystalline form: White powder

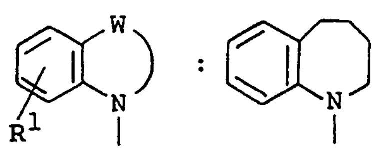
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 210 - 211°C

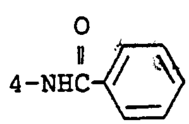
Form: Free

Example 132

Structure



R^2: H

R^3: 

Crystalline form: White powder

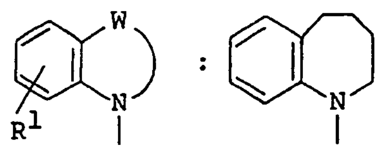
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 230.5 - 231.5°C

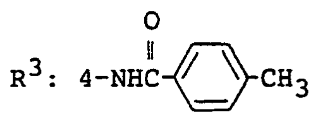
Form: Free

Example 133

Structure



R^2: H



Crystalline form: White powder

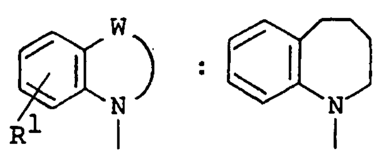
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 203 - 204°C

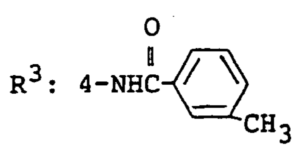
Form: Free

Example 134

Structure



R^2: H



Crystalline form: White powder

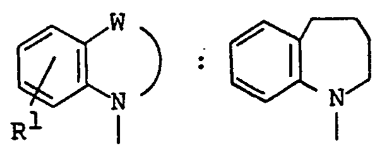
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 170 - 171°C

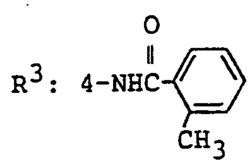
Form: Free

Example 135

Structure



R^2: H



Crystalline form: White powder

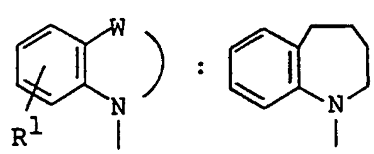
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 225.5 - 226.5°C

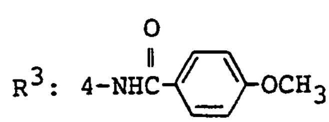
Form: Free

Example 136

Structure



R^2: H



Crystalline form: White powder

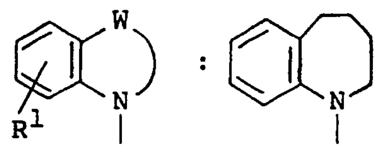
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 210.5 - 211.5°C

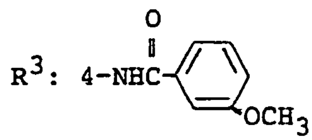
Form: Free

Example 137

Structure



R^2: H



Crystalline form: White powder

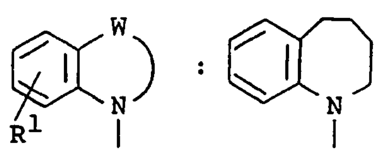
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 183 - 184°C

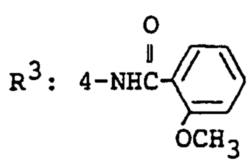
Form: Free

Example 138

Structure



R^2: H



Crystalline form: White powder

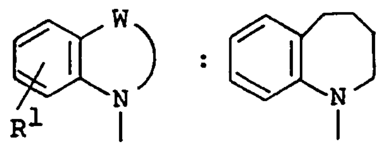
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 191.5 - 192.5°C

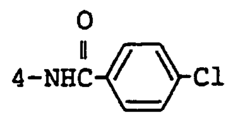
Form: Free

Example 139

Structure



R^2: H

R^3: 

Crystalline form: White powder

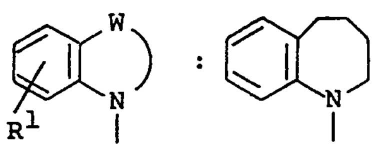
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 203.5 - 204.5°C

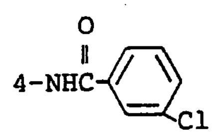
Form: Free

Example 140

Structure



R^2: H

R^3: 

Crystalline form: White powder

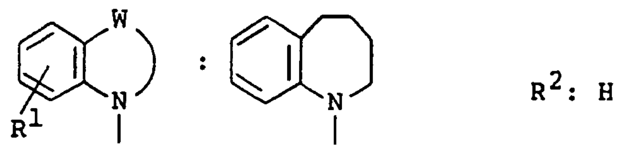
Recrystallization solvent: Ethanol/diethyl ether

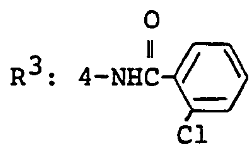
Melting Point: 215.5 - 216.5°C

Form: Free

Example 141

Structure





Crystalline form: White powder

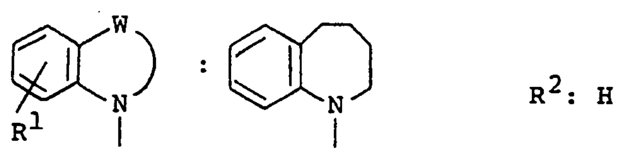
Recrystallization solvent: Ethanol/diethyl ether

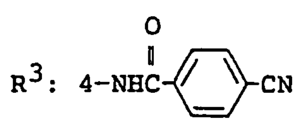
Melting Point: 211.5 - 212.5°C

Form: Free

Example 142

Structure





Crystalline form: White powder

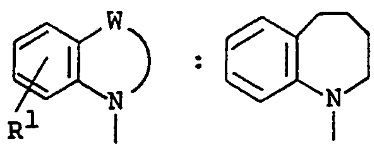
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 280.5 - 281.5°C

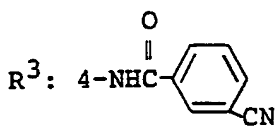
Form: Free

Example 143

Structure



R^2: H



Crystalline form: White powder

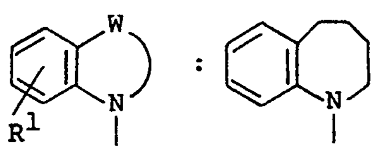
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 235.5 - 236.5°C

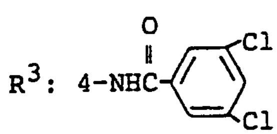
Form: Free

Example 144

Structure



R^2: H



Crystalline form: White powder

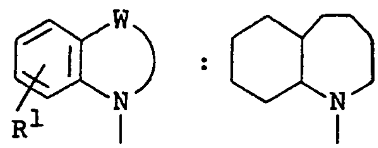
Recrystallization solvent: Ethanol/dichloromethane

Melting Point: 249.5 - 250.5°C

Form: Free

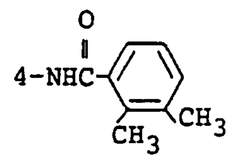
Example 145

Structure



R^2: H

R^3:



Crystalline form: White powder

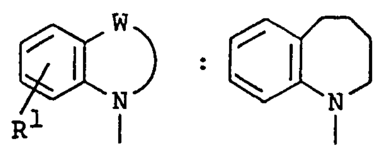
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 217 - 218°C

Form: Free

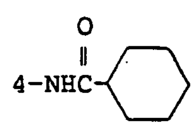
Example 146

Structure



R^2: 3-CH_3

R^3:



Crystalline form: White powder

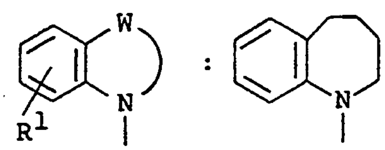
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 201.5 - 203°C

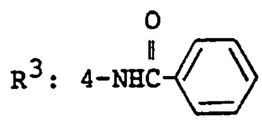
Form: Free

Example 147

Structure



R^2: 3-CH_3



Crystalline form: White powder

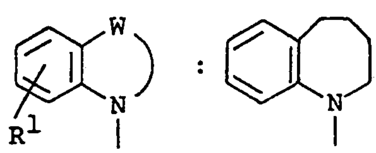
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 221 - 222°C

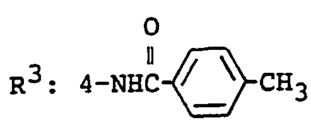
Form: Free

Example 148

Structure



R^2: 3-CH_3



Crystalline form: White powder

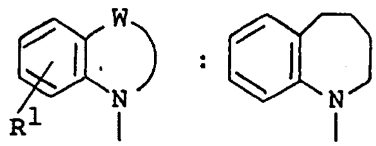
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 193 - 194°C

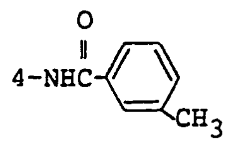
Form: Free

Example 149

Structure



R^2: 3-CH_3

R^3: 

Crystalline form: White powder

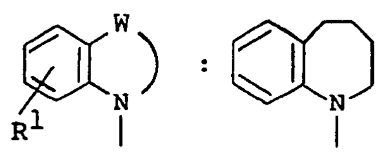
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 176 - 177°C

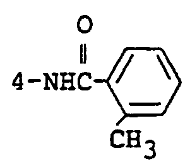
Form: Free

Example 150

Structure



R^2: 3-CH_3

R^3: 

Crystalline form: White powder

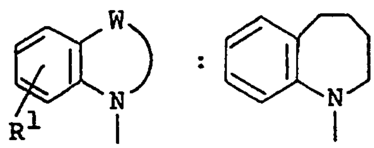
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 188 - 189.5°C

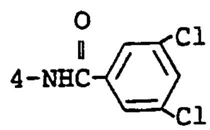
Form: Free

Example 151

Structure



R^2: 3-CH_3

R^3: 

Crystalline form: White powder

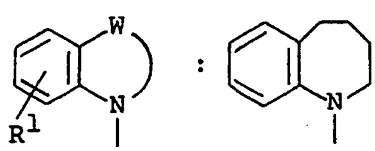
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 227 - 228°C

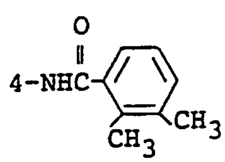
Form: Free

Example 152

Structure



R^2: 3-CH_3

R^3: 

Crystalline form: White powder

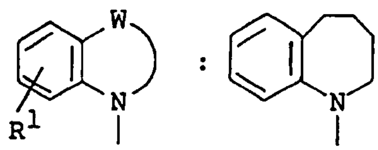
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 186 - 187°C

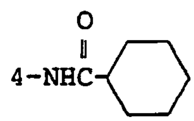
Form: Free

Example 153

Structure



R^2: 3-OCH_3

R^3: 

Crystalline form: White powder

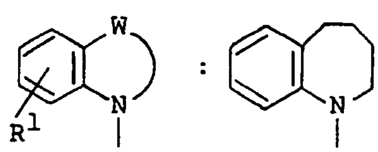
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 135 - 136°C

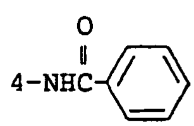
Form: Free

Example 154

Structure



R^2: 3-OCH_3

R^3: 

Crystalline form: White powder

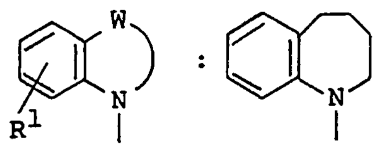
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 173 - 174°C

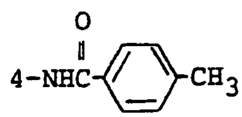
Form: Free

Example 155

Structure



R^2: 3-OCH_3

R^3: 

Crystalline form: White powder

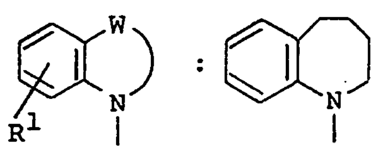
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 174.5 - 175.5°C

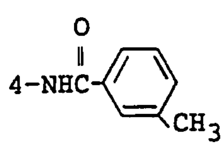
Form: Free

Example 156

Structure



R^2: 3-OCH_3

R^3: 

Crystalline form: White powder

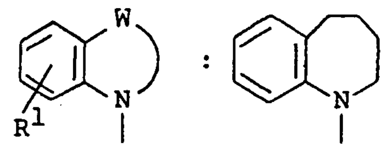
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 156 - 157°C

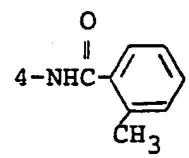
Form: Free

Example 157

Structure



R^2: 3-OCH_3

R^3: 

Crystalline form: White powder

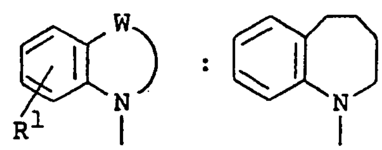
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 153 - 154°C

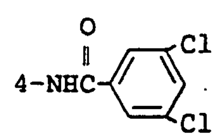
Form: Free

Example 158

Structure



R^2: 3-OCH_3

R^3: 

Crystalline form: White powder

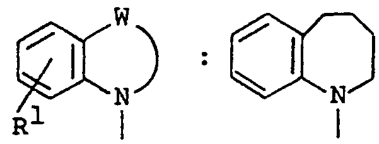
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 169 - 170°C

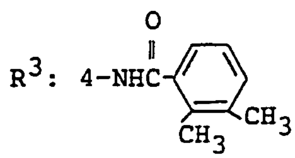
Form: Free.

Example 159

Structure



R^2: 3-OCH_3



Crystalline form: White powder

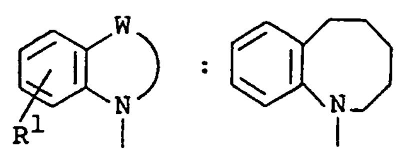
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 185 - 186°C

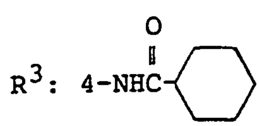
Form: Free

Example 160

Structure



R^2: H



Crystalline form: White powder

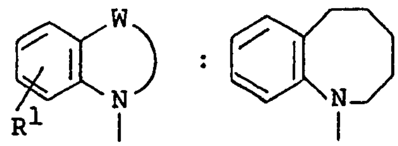
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 213 - 214°C

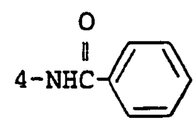
Form: Free

Example 161

Structure



R^2: H

R^3: 

Crystalline form: White powder

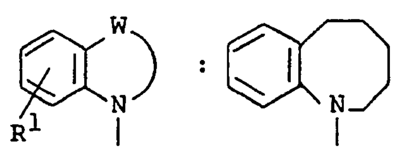
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 240 - 241°C

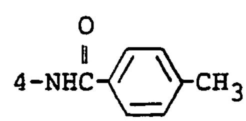
Form: Free

Example 162

Structure



R^2: H

R^3: 

Crystalline form: White powder

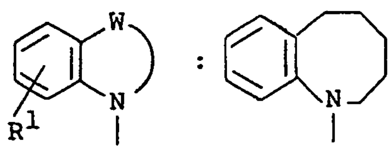
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 225 - 226°C

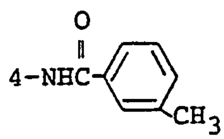
Form: Free

Example 163

Structure



R^2: H

R^3: 

Crystalline form: White powder

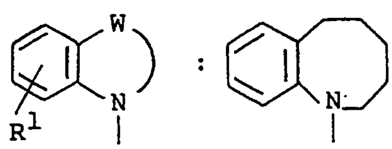
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 209.5 - 210.5°C

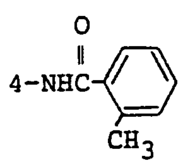
Form: Free

Example 164

Structure



R^2: H

R^3: 

Crystalline form: White powder

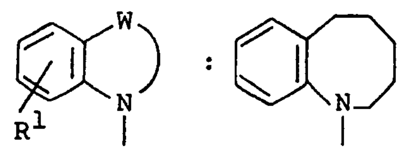
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 198 - 199°C

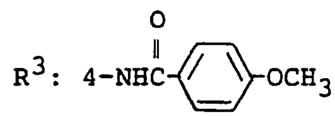
Form: Free

Example 165

Structure



R^2: H



Crystalline form: White powder

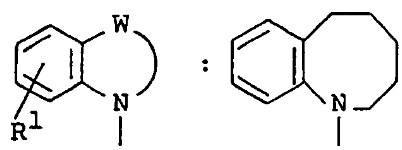
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 214.5 - 215.5°C

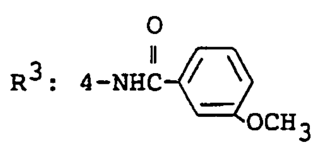
Form: Free

Example 166

Structure



R^2: H



Crystalline form: White powder

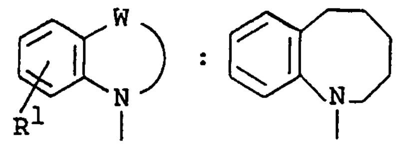
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 196.5 - 197.5°C

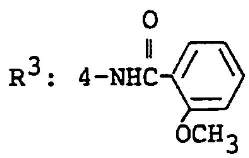
Form: Free

Example 167

Structure



R^2: H



Crystalline form: White powder

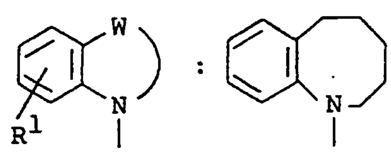
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 194 - 195°C

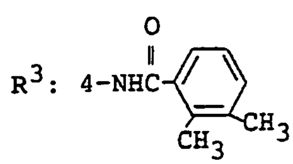
Form: Free

Example 168

Structure



R^2: H



Crystalline form: White powder

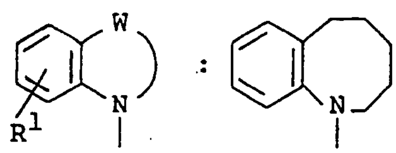
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 191 - 192°C

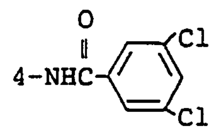
Form: Free

Example 169

Structure



R^2: H

R^3: 

Crystalline form: White powder

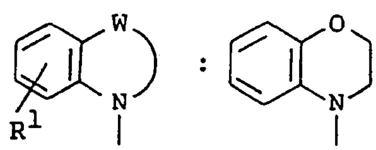
Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 227 - 228°C

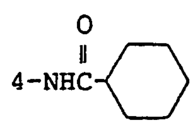
Form: Free

Example 170

Structure



R^2: H

R^3: 

Crystalline form: White powder

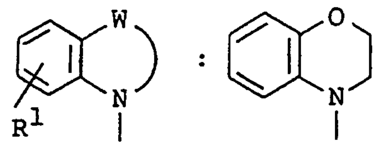
Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 182 - 183°C

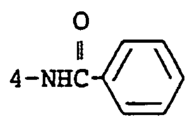
Form: Free

Example 171

Structure



R^2: H

R^3: 

Crystalline form: White powder

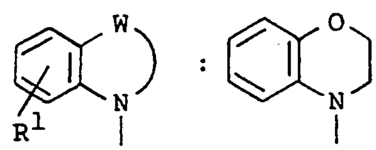
Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 222 - 223°C

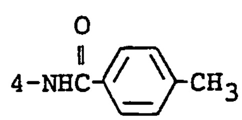
Form: Free

Example 172

Structure



R^2: H

R^3: 

Crystalline form: White powder

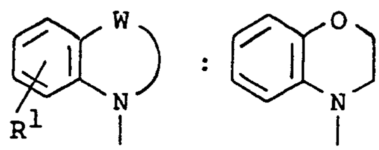
Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 204 - 205°C

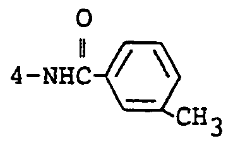
Form: Free

Example 173

Structure



R^2: H

R^3: 

Crystalline form: White powder

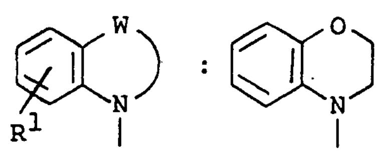
Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 194 - 195°C

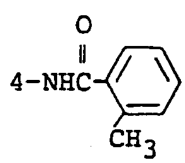
Form: Free

Example 174

Structure



R^2: H

R^3: 

Crystalline form: White powder

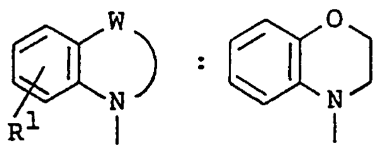
Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 213 - 214°C

Form: Free

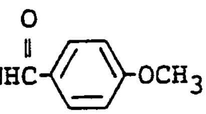
Example 175

Structure



R^2: H

R^3: 4-NHC-



Crystalline form: White powder

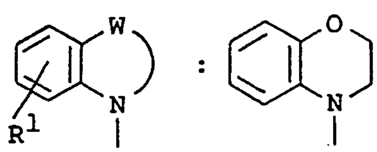
Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 201 - 202°C

Form: Free

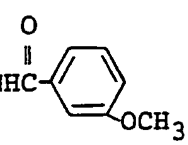
Example 176

Structure



R^2: H

R^3: 4-NHC-



Crystalline form: Colorless needles

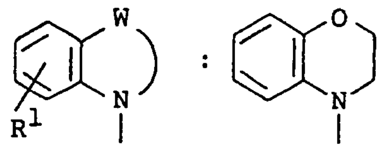
Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 173 - 174°C

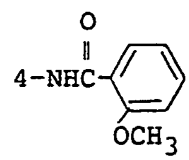
Form: Free

Example 177

Structure



R^2: H

R^3: 

Crystalline form: White powder

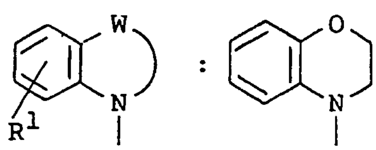
Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 150.5 - 151.5°C

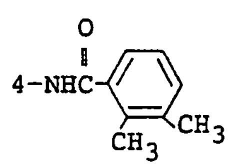
Form: Free

Example 178

Structure



R^2: H

R^3: 

Crystalline form: White powder

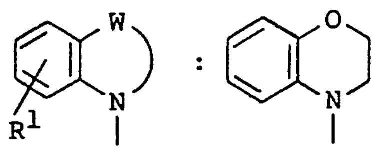
Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 207.5 - 208.5°C

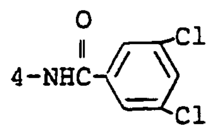
Form: Free

Example 179

Structure



R^2: H

R^3: 

Crystalline form: White powder

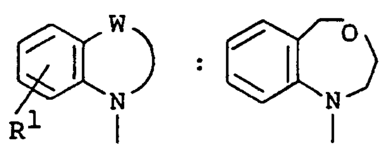
Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 256.5 - 257.5°C

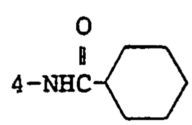
Form: Free

Example 180

Structure



R^2: H

R^3: 

Crystalline form: White powder

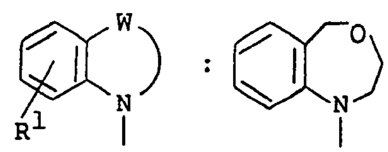
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 199.5 - 200.5°C

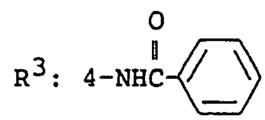
Form: Free

Example 181

Structure



R^2: H



Crystalline form: White powder

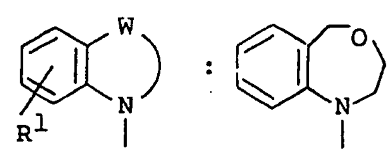
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 211 - 212°C

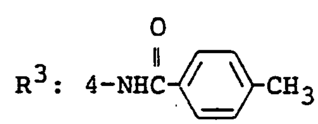
Form: Free

Example 182

Structure



R^2: H



Crystalline form: White powder

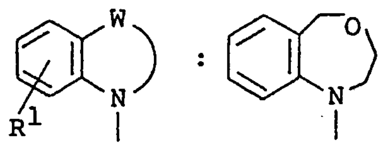
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 189.5 - 190.5°C

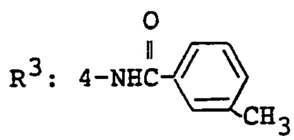
Form: Free

Example 183

Structure



R^2: H



Crystalline form: White powder

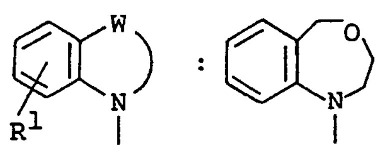
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 176.5 - 177.5°C

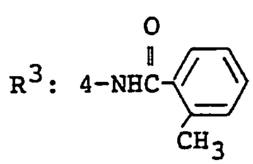
Form: Free

Example 184

Structure



R^2: H



Crystalline form: Yellow powder

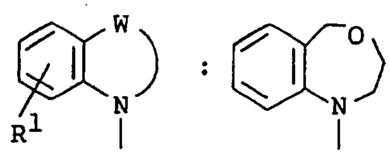
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 202 - 203°C

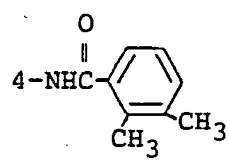
Form: Free

Example 185

Structure



R^2: H

R^3: 

Crystalline form: White powder

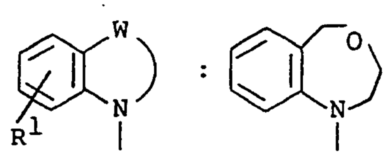
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 219 - 220°C

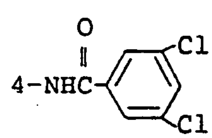
Form: Free

Example 186

Structure



R^2: H

R^3: 

Crystalline form: White powder

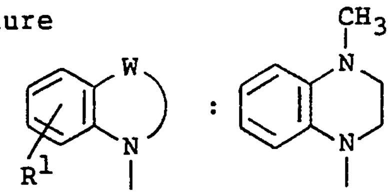
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 272 - 273°C

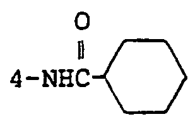
Form: Free

Example 187

Structure



R^2: H

R^3: 

Crystalline form: Yellow powder

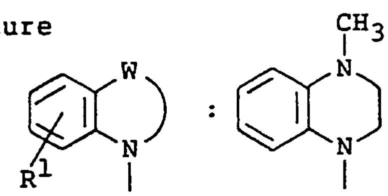
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 146 - 147°C

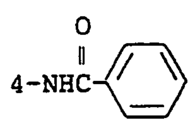
Form: Free

Example 188

Structure



R^2: H

R^3: 

Crystalline form: Yellow powder

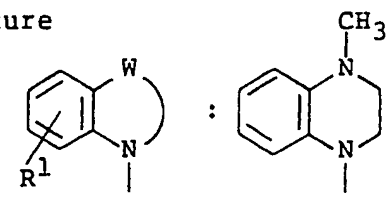
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 229.5 - 230.5°C

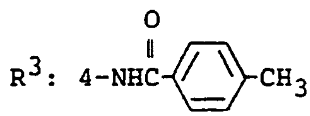
Form: Free

Example 189

Structure



R^2: H



Crystalline form: Yellow powder

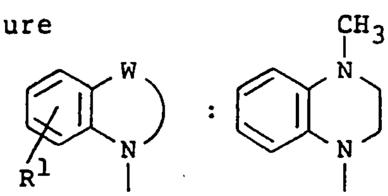
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 119.5 - 120.5°C

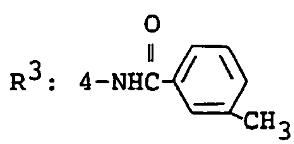
Form: Free

Example 190

Structure



R^2: H



Crystalline form: Yellow powder

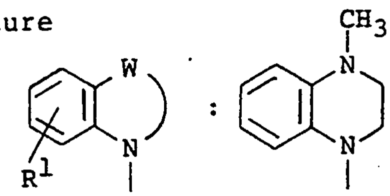
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 189 - 190°C

Form: Free

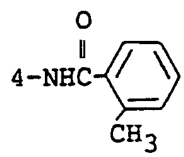
Example 191

Structure



R^2: H

R^3:



Crystalline form: Yellow powder

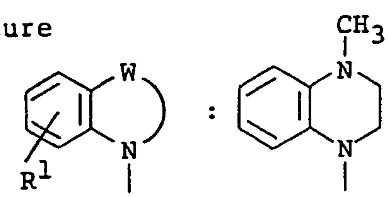
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 207 - 208°C

Form: Free

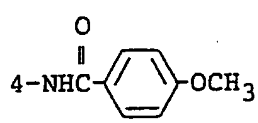
Example 192

Structure



R^2: H

R^3:



Crystalline form: Yellow powder

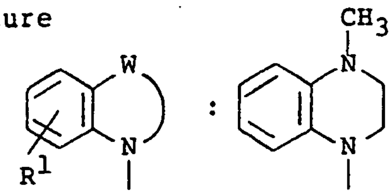
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 196.5 - 197.5°C

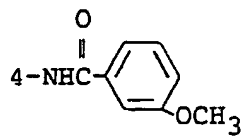
Form: Free

Example 193

Structure



R^2: H

R^3: 

Crystalline form: Yellow powder

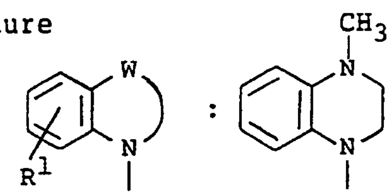
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 182 - 183°C

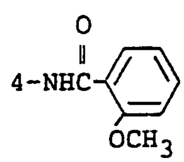
Form: Free

Example 194

Structure



R^2: H

R^3: 

Crystalline form: Yellow powder

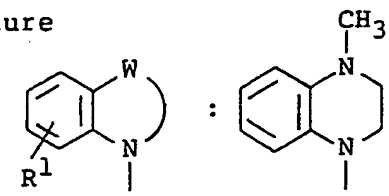
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 172 - 173°C

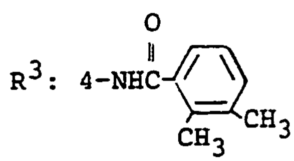
Form: Free

Example 195

Structure



R^2: H



Crystalline form: Yellow powder

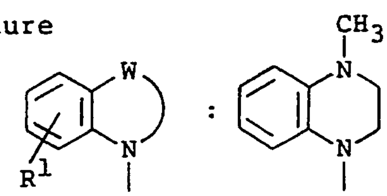
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 197.5 - 198.5°C

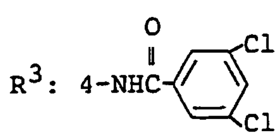
Form: Free

Example 196

Structure



R^2: H



Crystalline form: Yellow powder

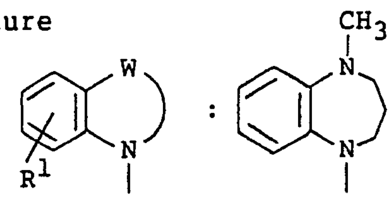
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 227 - 228°C

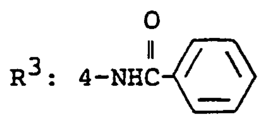
Form: Free

Example 197

Structure



R^2: H



Crystalline form: White powder

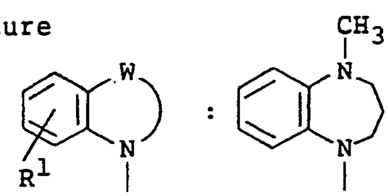
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 216.5 - 217.5°C

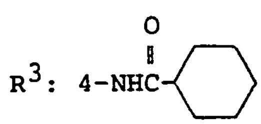
Form: Free

Example 198

Structure



R^2: H



Crystalline form: White powder

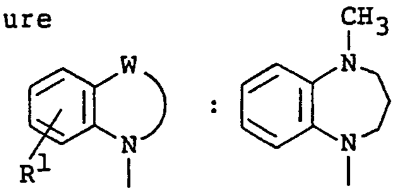
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 207 - 208°C

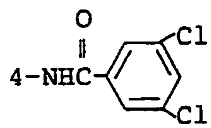
Form: Free

Example 199

Structure



R^2: H

R^3: 

Crystalline form: White powder

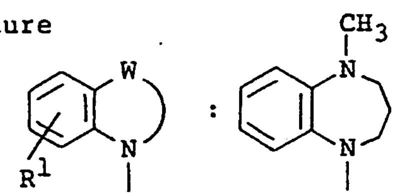
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 236 - 237°C

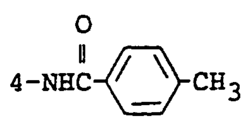
Form: Free

Example 200

Structure



R^2: H

R^3: 

Crystalline form: White powder

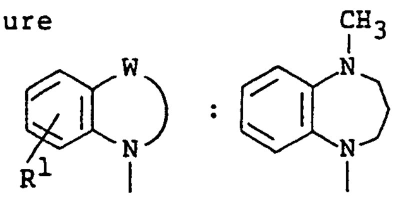
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 199.5 - 200.5°C

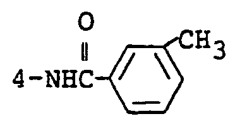
Form: Free

Example 201

Structure



R^2: H

R^3: 

Crystalline form: White powder

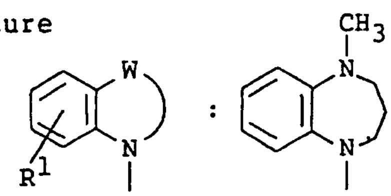
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 171.5 - 172.5°C

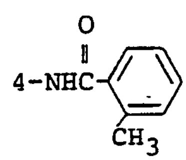
Form: Free

Example 202

Structure



R^2: H

R^3: 

Crystalline form: White powder

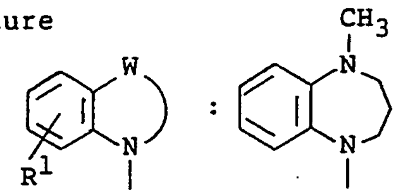
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 222.5 - 223.5°C

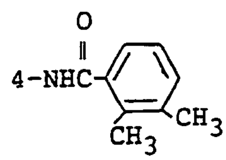
Form: Free

Example 203

Structure



R^2: H

R^3: 

Crystalline form: White powder

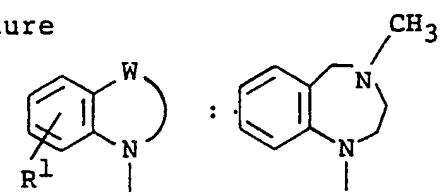
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 209.5 - 210.5°C

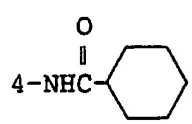
Form: Free

Example 204

Structure



R^2: H

R^3: 

Crystalline form: White powder

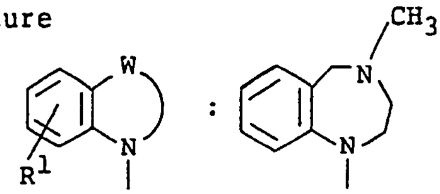
Recrystallization solvent: Ethanol/water

NMR analysis: 14)

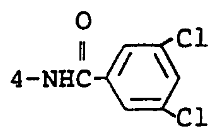
Form: Hydrochloride

Example 205

Structure



R^2: H

R^3: 

Crystalline form: White powder

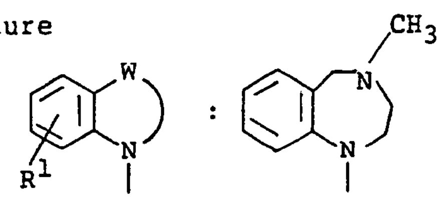
Recrystallization solvent: Ethanol/water

NMR analysis: 15)

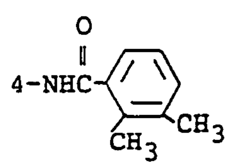
Form: Hydrochloride

Example 206

Structure



R^2: H

R^3: 

Crystalline form: White powder

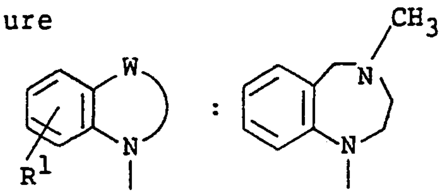
Recrystallization solvent: Ethanol/water

NMR analysis: 16)

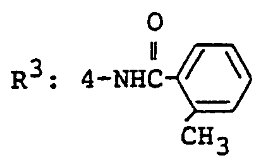
Form: Hydrochloride

Example 207

Structure



R^2: H



Crystalline form: White powder

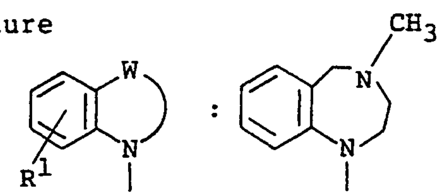
Recrystallization solvent: Ethanol/water

NMR analysis: 17)

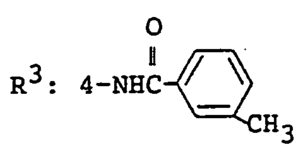
Form: Hydrochloride

Example 208

Structure



R^2: H



Crystalline form: White powder

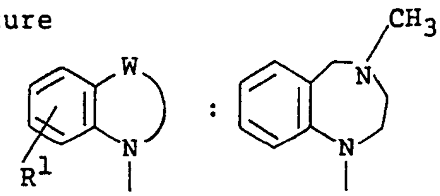
Recrystallization solvent: Ethanol/water

NMR analysis: 18)

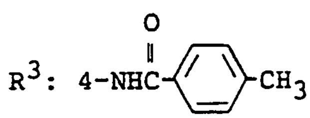
Form: Hydrochloride

Example 209

Structure



R^2: H



Crystalline form: Yellow powder

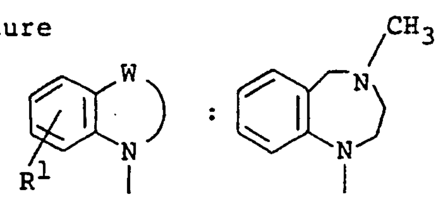
Recrystallization solvent: Ethanol/water

NMR analysis: 19)

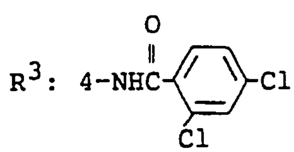
Form: Hydrochloride

Example 210

Structure



R^2: H



Crystalline form: White powder

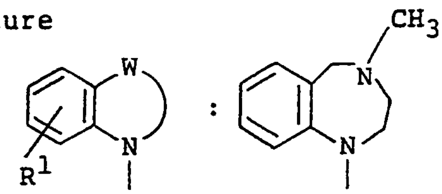
Recrystallization solvent: Ethanol/water

NMR analysis: 20)

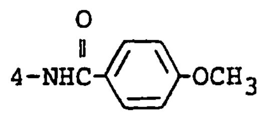
Form: Hydrochloride

Example 211

Structure



R^2: H

R^3: 

Crystalline form: White powder

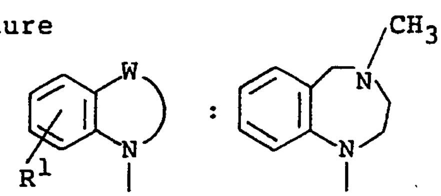
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 159.5 - 160.5°C

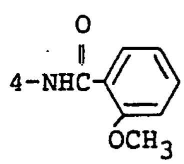
Form: Free

Example 212

Structure



R^2: H

R^3: 

Crystalline form: White powder

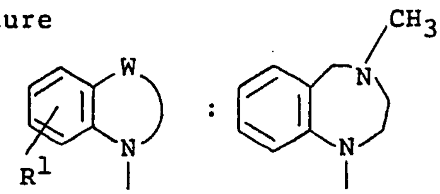
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 189.5 - 190.5°C

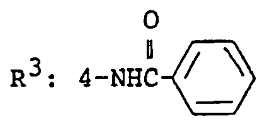
Form: Free.

Example 213

Structure



R^2: H



Crystalline form: White powder

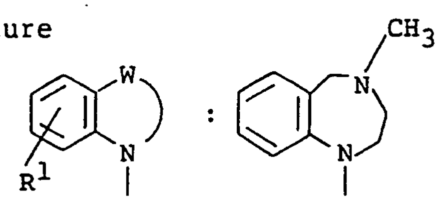
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 170.5 - 171.5°C

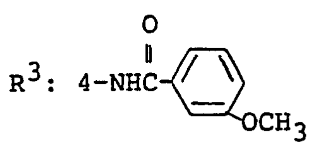
Form: Free

Example 214

Structure



R^2: H



Crystalline form: White powder

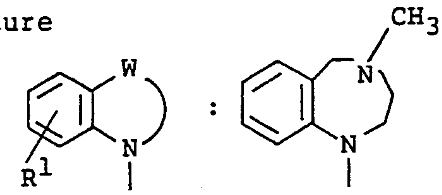
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 165 - 166°C

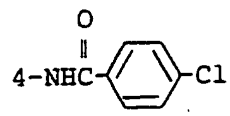
Form: Free

Example 215

Structure



R^2: H

R^3: 

Crystalline form: White powder

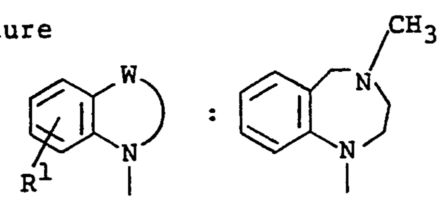
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 173.5 - 174.5°C

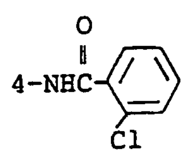
Form: Free

Example 216

Structure



R^2: H

R^3: 

Crystalline form: White powder

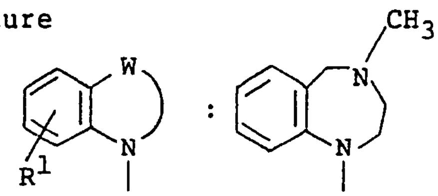
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 182 - 183°C

Form: Free

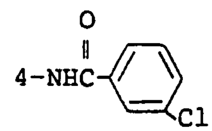
Example 217

Structure



R^2: H

R^3:



Crystalline form: White powder

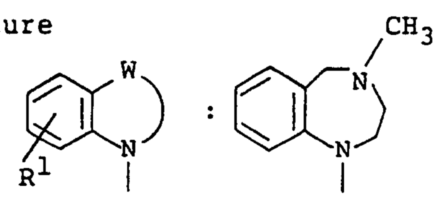
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 225.5 - 226.5°C

Form: Free

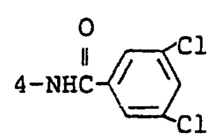
Example 219

Structure



R^2: 3-OCH_3

R^3:



Crystalline form: White powder

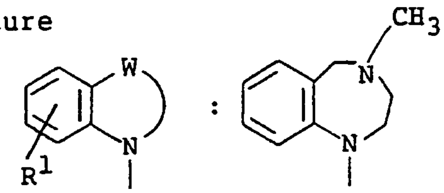
Recrystallization solvent: Ethanol/water

NMR analysis: 21)

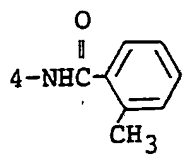
Form: Hydrochloride

Example 220

Structure



R^2: 3-OCH_3

R^3: 

Crystalline form: White powderr

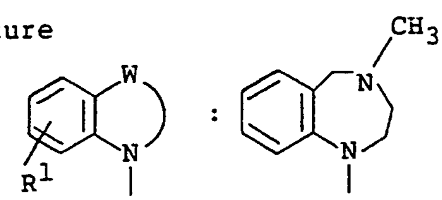
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 147.5 - 148.5°C

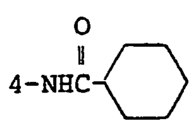
Form: Free

Example 221

Structure



R^2: 3-OCH_3

R^3: 

Crystalline form: White powder

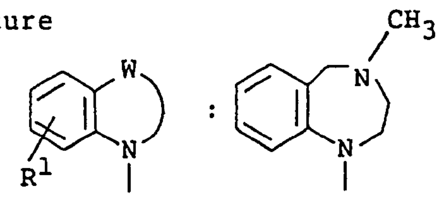
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 136 - 137°C

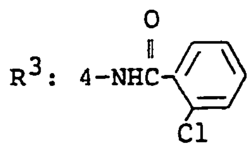
Form: Free

Example 222

Structure



R^2: 3-OCH_3



Crystalline form: White powder

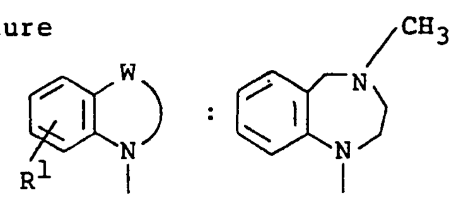
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 191.5 - 192.5°C

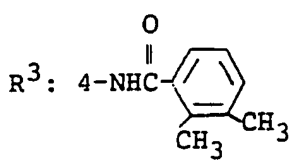
Form: Free

Example 223

Structure



R^2: 3-OCH_3



Crystalline form: White powder

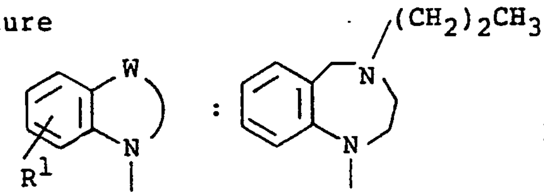
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 145 - 146°C

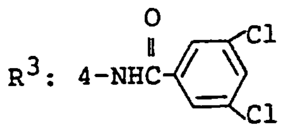
Form: Free

Example 224

Structure



R^2: H



Crystalline form: White powder

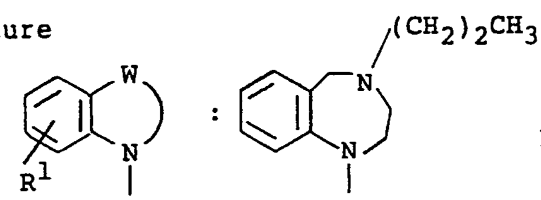
Recrystallization solvent: Ethanol/water

NMR analysis: 22)

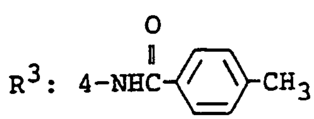
Form: Hydrochloride

Example 225

Structure



R^2: H



Crystalline form: White powder

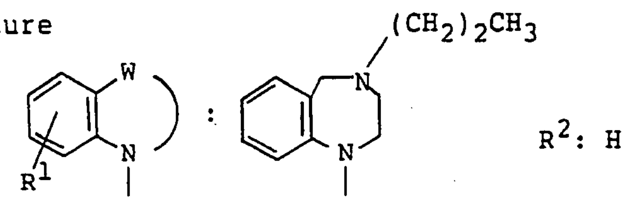
Recrystallization solvent: Ethanol/water

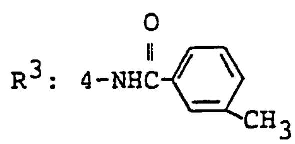
NMR analysis: 23)

Form: Hydrochloride

Example 226

Structure





Crystalline form: White powder

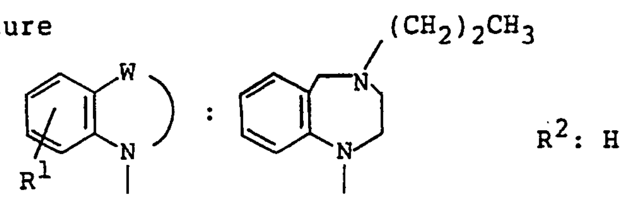
Recrystallization solvent: Ethanol/water

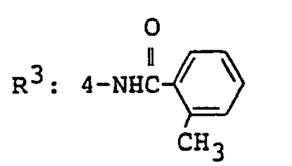
NMR analysis: 24)

Form: Hydrochloride

Example 227

Structure





Crystalline form: White powder

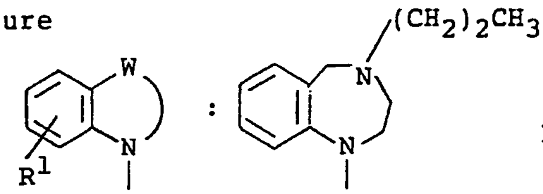
Recrystallization solvent: Ethanol/water

NMR analysis: 25)

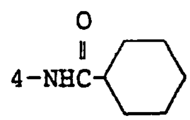
Form: Hydrochloride

Example 228

Structure



R^2: H

R^3: 

Crystalline form: White powder

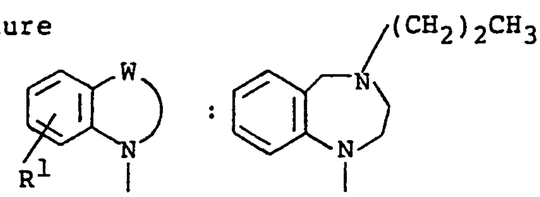
Recrystallization solvent: Ethanol/water

NMR analysis: 26)

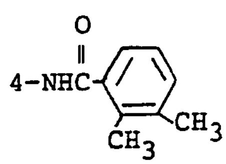
Form: Hydrochloride

Example 229

Structure



R^2: H

R^3: 

Crystalline form: White powder

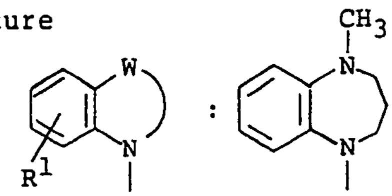
Recrystallization solvent: Ethanol/water

NMR analysis: 27)

Form: Hydrochloride

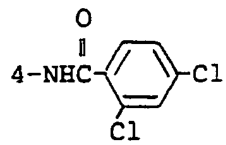
Example 230

Structure



R^2: H

R^3:



Crystalline form: White powder

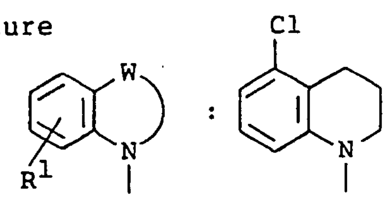
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 206 - 207°C

Form: Free

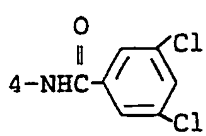
Example 231

Structure



R^2: H

R^3:



Crystalline form: White powder

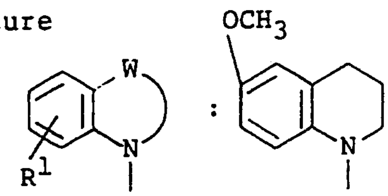
Recrystallization solvent: Chloroform/methanol

Melting Point: 211 - 213°C

Form: Free

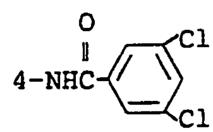
Example 232

Structure



R^2: H

R^3: 4-NHC-



Crystalline form: White powder

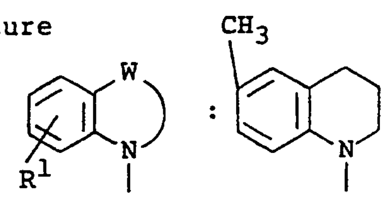
Recrystallization solvent: Chloroform/methanol

Melting Point: 228.5 - 229.5°C

Form: Free

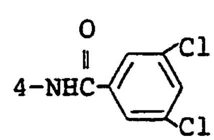
Example 233

Structure



R^2: H

R^3: 4-NHC-



Crystalline form: White powder

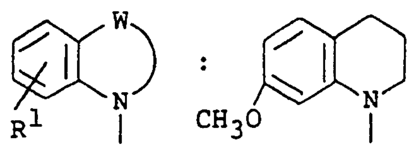
Recrystallization solvent: Chloroform/methanol

Melting Point: 237 - 238°C

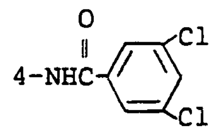
Form: Free

Example 234

Structure



R^2: H

R^3: 

Crystalline form: White powder

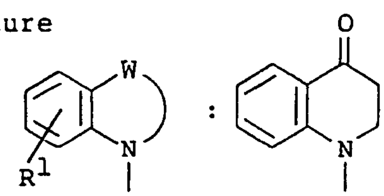
Recrystallization solvent: Chloroform/methanol

Melting Point: 226 - 228°C

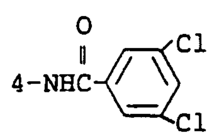
Form: Free

Example 235

Structure



R^2: H

R^3: 

Crystalline form: White powder

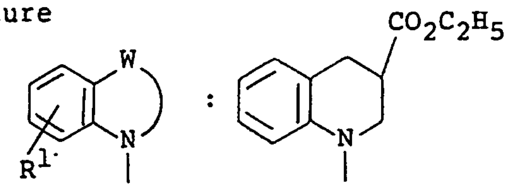
Recrystallization solvent: Chloroform/methanol

Melting Point: 220 - 222°C

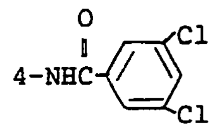
Form: Free

Example 236

Structure



R^2: H

R^3: 

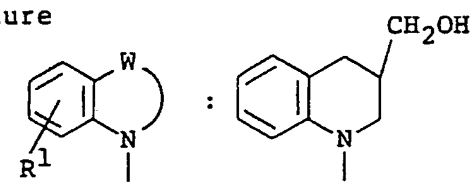
Crystalline form: Colorless amorphous

NMR analysis: 28)

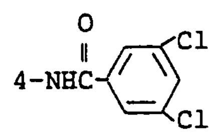
Form: Free

Example 237

Structure



R^2: H

R^3: 

Crystalline form: White powder

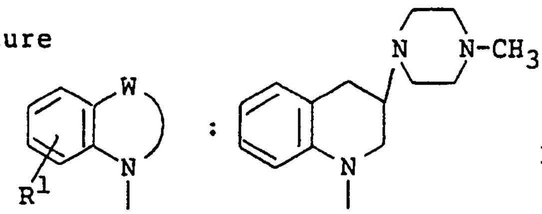
Recrystallization solvent: Ethanol

Melting Point: 162 - 165°C

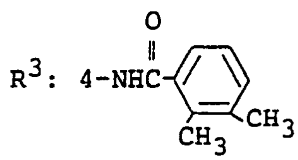
Form: Free

Example 238

Structure



R^2: H



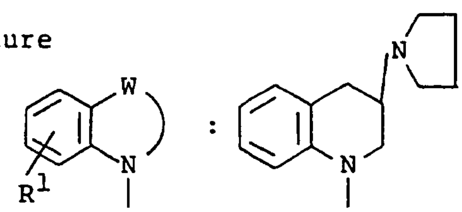
Crystalline form: Light brown amorphous

NMR analysis: 29)

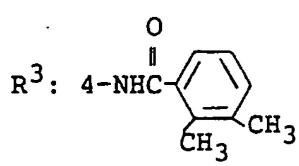
Form: Free

Example 239

Structure



R^2: H



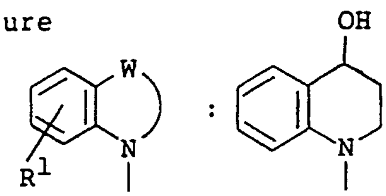
Crystalline form: Light brown amorphous

NMR analysis: 30)

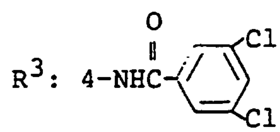
Form: Free

Example 240

Structure



R^2: H



Crystalline form: White powder

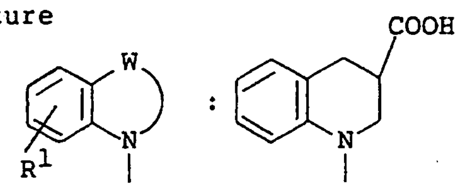
Recrystallization solvent: Ethanol

Melting Point: 215 - 217°C

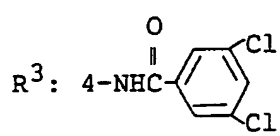
Form: Free

Example 241

Structure



R^2: H



Crystalline form: White powder

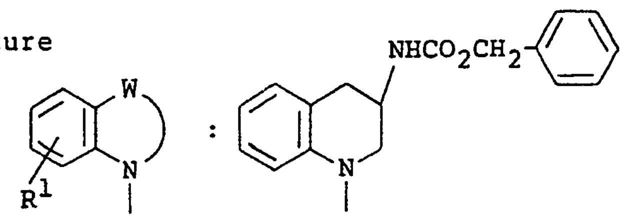
Recrystallization solvent: Ethanol

Melting Point: 221 - 223°C

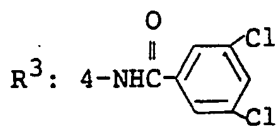
Form: Free

Example 242

Structure



R^2: H



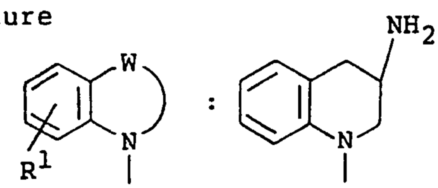
Crystalline form: Colorless amorphous

NMR analysis: 31)

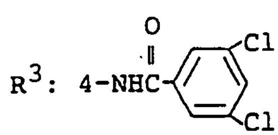
Form: Free

Example 243

Structure



R^2: H



Crystalline form: White powder

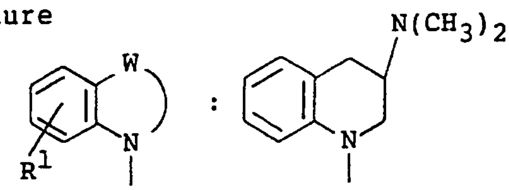
Recrystallization solvent: Ethanol

Melting Point: 207 - 210°C

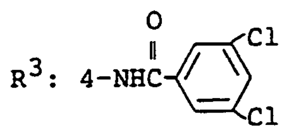
Form: Free

Example 244

Structure



R^2: H



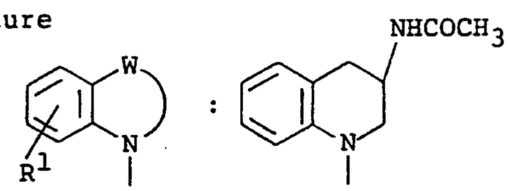
Crystalline form: Colorless amorphous

NMR analysis: 32)

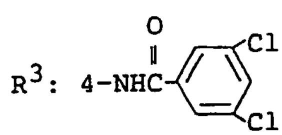
Form: Free

Example 245

Structure



R^2: H



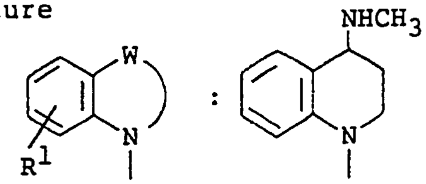
Crystalline form: Colorless amorphous

NMR analysis: 33)

Form: Free

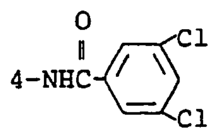
Example 246

Structure



R^2: H

R^3:



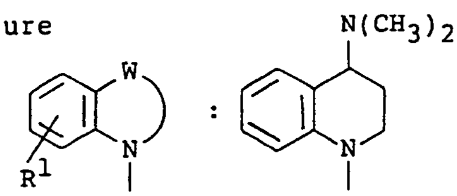
Crystalline form: Colorless amorphous

NMR analysis: 34)

Form: Free

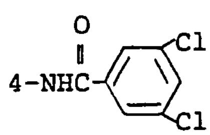
Example 247

Structure



R^2: H

R^3:



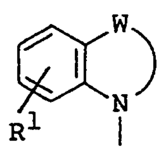
Crystalline form: Colorless amorphous

NMR analysis: 35)

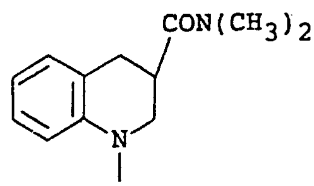
Form: Free

Example 248

Structure

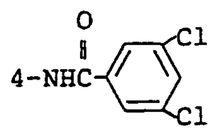


:



R^2: H

R^3:



Crystalline form: Light yellow powder

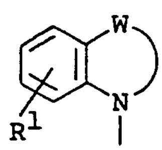
Recrystallization solvent: Ethanol

Melting Point: 186 - 187°C

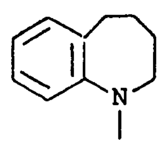
Form: Free

Example 249

Structure

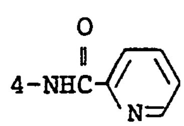


:



R^2: H

R^3:



Crystalline form: Colorless needles

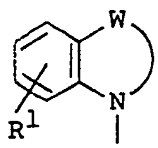
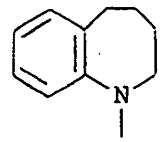
Recrystallization solvent: Ethanol

Melting Point: 190 - 191°C

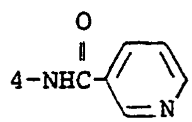
Form: Free

Example 250

Structure

 : 

R^2: H

R^3: 

Crystalline form: Light yellow scales

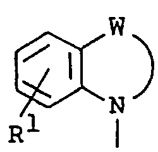
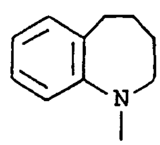
Recrystallization solvent: Ethanol/water

Melting Point: 230 - 231°C

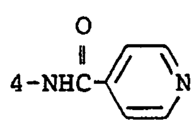
Form: Free

Example 251

Structure

 : 

R^2: H

R^3: 

Crystalline form: Light yellow needles

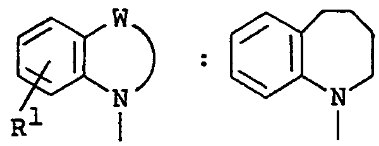
Recrystallization solvent: Ethanol

Melting Point: 227 - 228°C

Form: Free

Example 252

Structure



R^2: H

R^3: 4-$NH\overset{O}{\overset{\|}{C}}CH_2CH_2COOH$

Crystalline form: Colorless needles

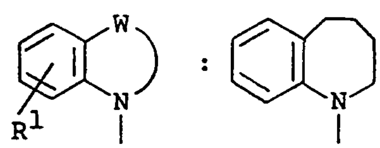
Recrystallization solvent: Ethyl acetate

Melting Point: 192°C

Form: Free

Example 253

Structure



R^2: H

R^3: 4-$NH\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2COOH$

Crystalline form: White powder

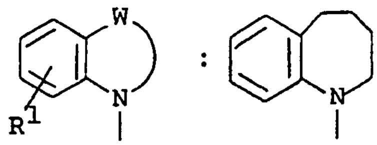
Recrystallization solvent: Ethyl acetate

Melting Point: 186.5 - 189°C

Form: Free

Example 254

Structure



R^2: H

R^3: $4\text{-NH}\overset{\overset{\text{O}}{\|}}{\text{C}}(\text{CH}_2)_2\overset{\overset{\text{O}}{\|}}{\text{C}}\text{N}(\text{C}_2\text{H}_5)_2$

Crystalline form: Light yellow scales

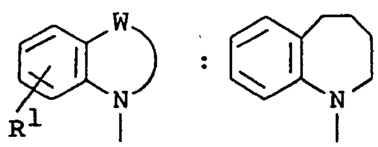
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 165 - 167°C

Form: Free

Example 255

Structure



R^2: H

R^3: $4\text{-NH}\overset{\overset{\text{O}}{\|}}{\text{C}}(\text{CH}_2)_2\overset{\overset{\text{O}}{\|}}{\text{C}}\text{NH}(\text{CH}_2)_3\text{CH}_3$

Crystalline form: White powder

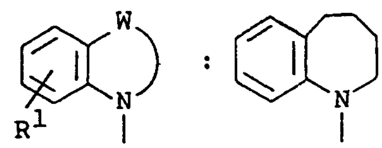
Recrystallization solvent: Ethyl acetate

Melting Point: 169 - 170°C

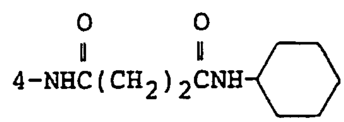
Form: Free

Example 256

Structure



R^2: H

R^3: 

Crystalline form: Colorless scales

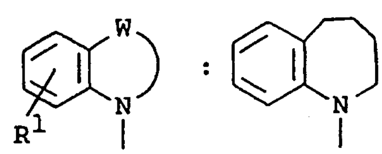
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 174 - 177°C

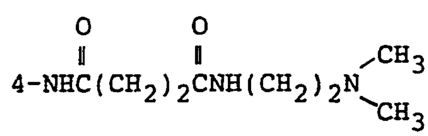
Form: Free

Example 257

Structure



R^2: H

R^3: 

Crystalline form: White powder

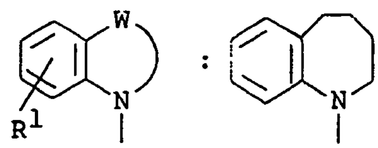
Recrystallization solvent: Ethyl acetate

Melting Point: 114 - 118°C

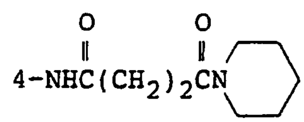
Form: Free

Example 258

Structure



R^2: H

R^3: 

Crystalline form: White powder

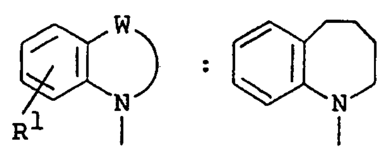
Recrystallization solvent: Ethyl acetate

Melting Point: 170 - 172°C

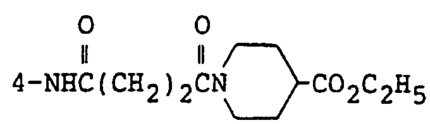
Form: Free

Example 259

Structure



R^2: H

R^3: 

Crystalline form: White powder

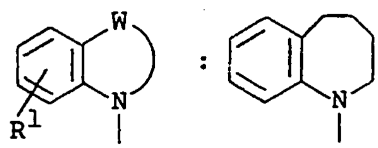
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 179 - 181°C

Form: Free

Example 260

Structure



R^2: H

R^3: $4\text{-}NH\overset{O}{\overset{\|}{C}}(CH_2)_2\overset{O}{\overset{\|}{C}}NH_2$

Crystalline form: White powder

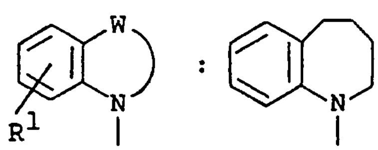
Recrystallization solvent: Ethyl acetate

Melting Point: 118 - 121°C

Form: Free

Example 261

Structure



R^2: H

R^3: $4\text{-}NH\overset{O}{\overset{\|}{C}}(CH_2)_3\overset{O}{\overset{\|}{C}}N(C_2H_5)_2$

Crystalline form: White powder

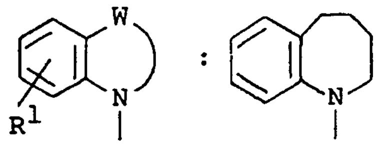
Recrystallization solvent: Ethyl acetate

Melting Point: 144 - 148°C

Form: Free

Example 262

Structure



R^2: H

R^3: $4\text{-NHC(=O)}(CH_2)_3\text{C(=O)NH}(CH_2)_3CH_3$

Crystalline form: Colorless scales

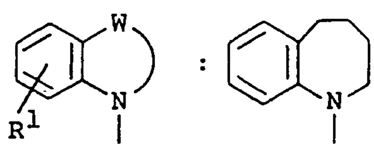
Recrystallization solvent: Ethyl acetate

Melting Point: 156 - 157°C

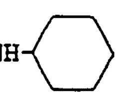
Form: Free

Example 263

Structure



R^2: H

R^3: $4\text{-NHC(=O)}(CH_2)_3\text{C(=O)NH-}$ 

Crystalline form: White powder

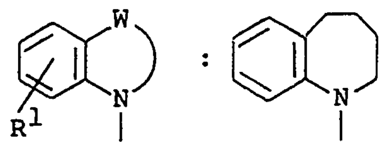
Recrystallization solvent: Ethyl acetate

Melting Point: 204 - 206°C

Form: Free

Example 264

Structure



R^2: H

R^3: $\mathrm{4\text{-}NH\overset{\overset{O}{\|}}{C}CH_2Cl}$

Crystalline form: Light yellow powder

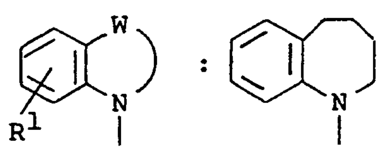
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 165 - 167°C

Form: Free

Example 265

Structure



R^2: H

R^3: $\mathrm{4\text{-}NH\overset{\overset{O}{\|}}{C}CH_2CH_2Cl}$

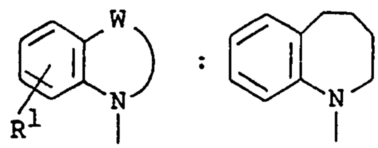
Crystalline form: Light yellow amorphous

NMR analysis: 36)

Form: Free

Example 266

Structure



R^2: H

R^3: 4-$\mathrm{NH\overset{\overset{O}{\|}}{C}(CH_2)_3Cl}$

Crystalline form: White powder

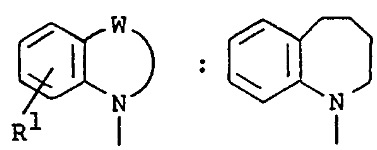
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 122 - 124°C

Form: Free

Example 267

Structure



R^2: H

R^3: 4-$\mathrm{NH\overset{\overset{O}{\|}}{C}CH_2CO_2C_2H_5}$

Crystalline form: Light yellow powder

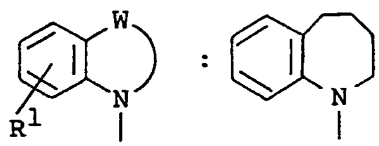
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 116 - 117°C

Form: Free

Example 268

Structure



R^2: H

R^3: $4\text{-NH}\overset{\overset{\displaystyle O}{\|}}{C}(CH_2)_2CO_2C_2H_5$

Crystalline form: White powder

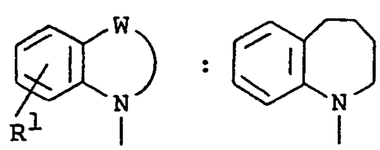
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 121 - 123°C

Form: Free

Example 269

Structure



R^2: H

R^3: $4\text{-NH}\overset{\overset{\displaystyle O}{\|}}{C}\text{-}\overset{\overset{\displaystyle Br}{|}}{C}H\text{-}C_2H_5$

Crystalline form: Colorless needles

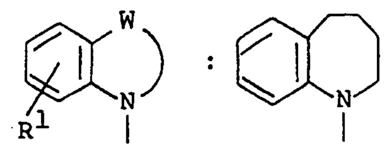
Recrystallization solvent: Ethyl acetate

Melting Point: 186 - 187°C

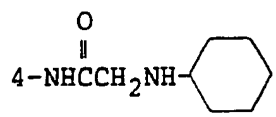
Form: Free

Example 270

Structure



R^2: H

R^3: 

Crystalline form: White powder

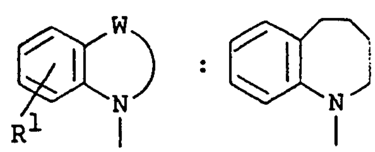
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 139 - 142°C

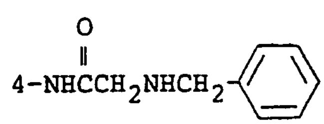
Form: Free

Example 271

Structure



R^2: H

R^3: 

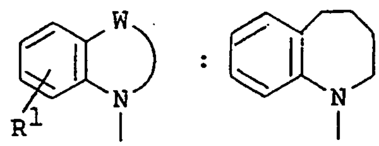
Crystalline form: Light yellow amorphous

NMR analysis: 37)

Form: Free

Example 272

Structure



R^2: H

R^3: 4-NHC(=O)CH$_2$NHCH(CH$_3$)$_2$

Crystalline form: White powder

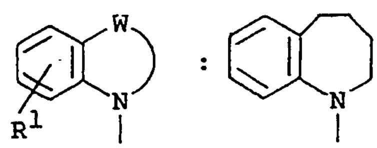
Recrystallization solvent: Ethyl acetate

Melting Point: 149.5 - 152.5°C

Form: Free

Example 273

Structure



R^2: H

R^3: 4-NHC(=O)CH$_2$NHC(CH$_3$)$_3$

Crystalline form: Colorless needles

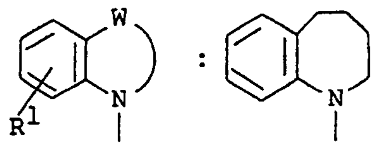
Recrystallization solvent: Ethanol

Melting Point: 150 - 152.5°C

Form: Free

Example 274

Structure



R^2: H

R^3: 4-$NHC(=O)CH_2NH(CH_2)_2OH$

Crystalline form: White powder

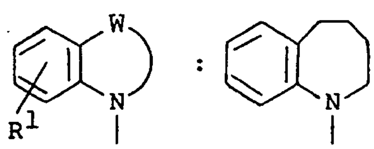
Recrystallization solvent: Ethyl acetate

Melting Point: 150°C

Form: Free

Example 275

Structure



R^2: H

R^3: 4-$NHC(=O)CH_2N(C_2H_5)_2$

Crystalline form: Colorless needles

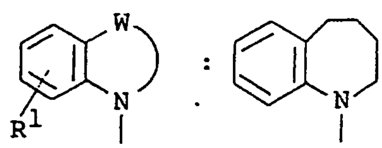
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 101 - 104°C

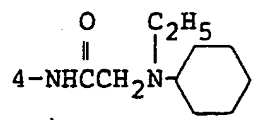
Form: Free

Example 276

Structure



R^2: H

R^3: 

Crystalline form: White powder

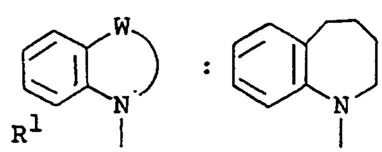
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 120 - 122°C

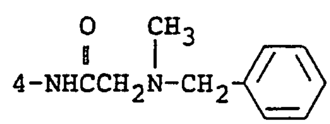
Form: Free

Example 277

Structure



R^2: H

R^3: 

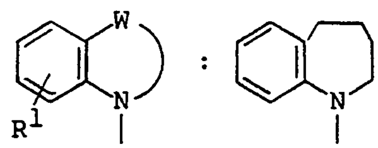
Crystalline form: Light yellow amorphous

NMR analysis: 38)

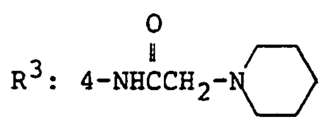
Form: Free

Example 278

Structure



R^2: H



Crystalline form: Colorless needles

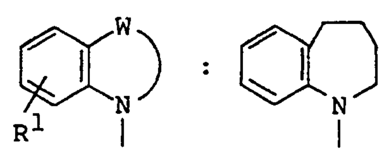
Recrystallization solvent: Ethanol

Melting Point: 183 - 186°C

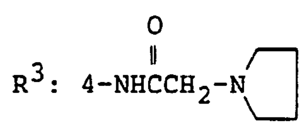
Form: Free

Example 279

Structure



R^2: H



Crystalline form: Light brown powder

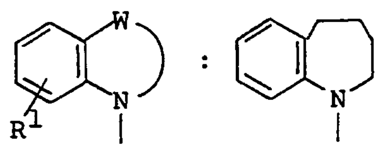
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 139 - 142°C

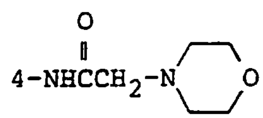
Form: Free

Example 280

Structure



R^2: H

R^3: 

Crystalline form: Light yellow powder

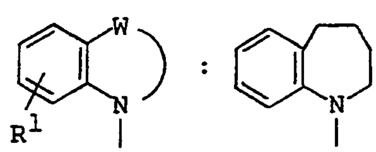
Recrystallization solvent: Ethanol

Melting Point: 162 - 165°C

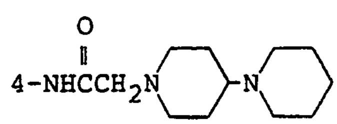
Form: Free

Example 281

Structure



R^2: H

R^3: 

Crystalline form: Light yellow scales

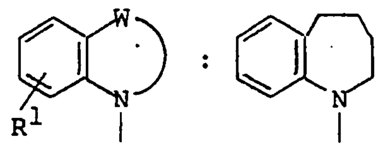
Recrystallization solvent: Ethyl acetate

Melting Point: 224 - 227°C

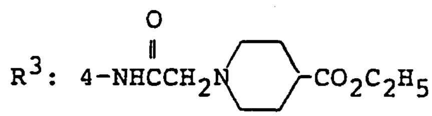
Form: Free

Example 282

Structure



R^2: H



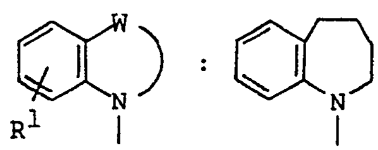
Crystalline form: Light yellow amorphous

NMR analysis: 39)

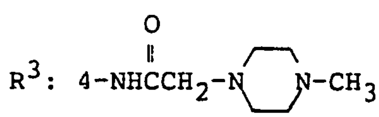
Form: Free

Example 283

Structure



R^2: H



Crystalline form: Light yellow powder

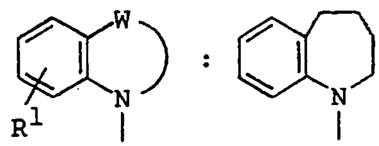
Recrystallization solvent: Ethanol/water

Melting Point: 162 - 164°C

Form: Free

Example 284

Structure



R^2: H

R^3: 4-$NH\overset{O}{\overset{\parallel}{C}}CH_2NH_2$

Crystalline form: Light yellow powder

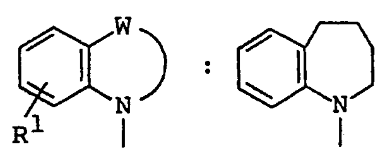
Recrystallization solvent: Ethanol

Melting Point: 238 - 241°C (decomposed)

Form: Hydrochloride

Example 285

Structure



R^2: H

R^3: 4-$NH\overset{O}{\overset{\parallel}{C}}CH_2NH\overset{O}{\overset{\parallel}{C}}CH_3$

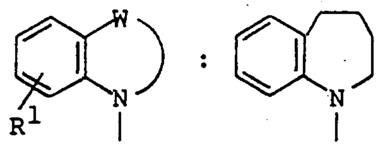
Crystalline form: Light yellow amorphous

NMR analysis: 40)

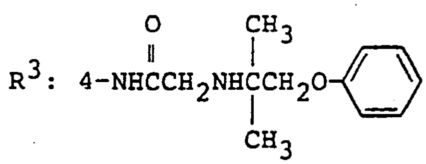
Form: Free

Example 286

Structure



R^2: H



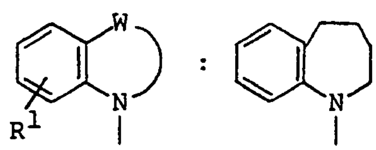
Crystalline form: Colorless amorphous

NMR analysis: 41)

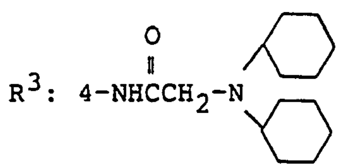
Form: Free

Example 287

Structure



R^2: H



Crystalline form: Colorless needles

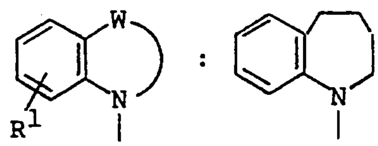
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 168 - 169°C

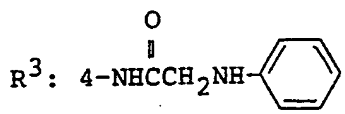
Form: Free

Example 288

Structure



R^2: H



Crystalline form: Light brown powder

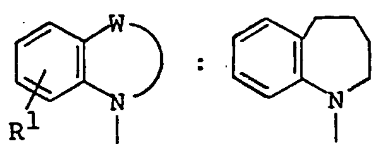
Recrystallization solvent: Ethanol

Melting Point: 189 - 191°C

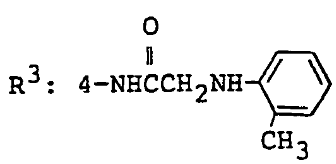
Form: Free

Example 289

Structure



R^2: H



Crystalline form: White powder

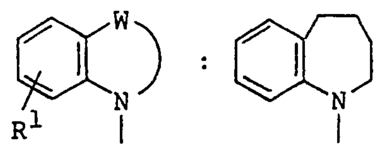
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 200 - 202°C

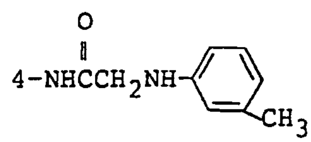
Form: Free

Example 290

Structure



R^2: H

R^3: 

Crystalline form: Colorless scales

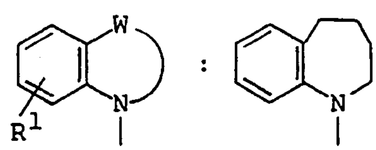
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 143 - 146°C

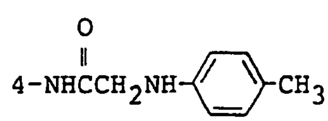
Form: Free

Example 291

Structure



R^2: H

R^3: 

Crystalline form: White powder

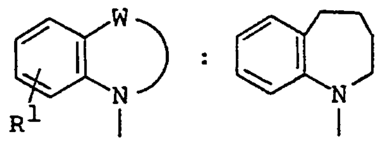
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 117 - 117.5°C

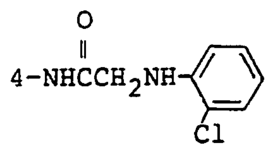
Form: Free

Example 292

Structure



R^2: H

R^3: 

Crystalline form: Light brown powder

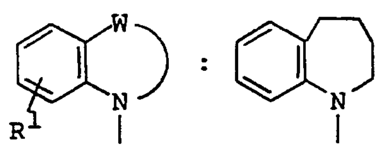
Recrystallization solvent: Diethyl ether/ethyl acetate

Melting Point: 225 - 226°C

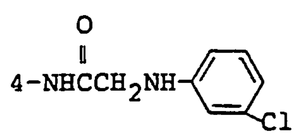
Form: Free

Example 293

Structure



R^2: H

R^3: 

Crystalline form: White powder

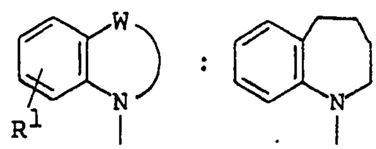
Recrystallization solvent: n-Hexane/ethanol

Melting Point: 175 - 176.5°C

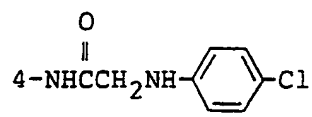
Form: Free

Example 294

Structure



R^2: H

R^3: 

Crystalline form: White powder

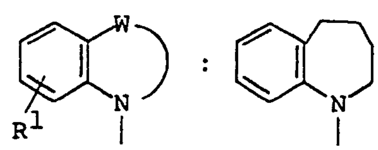
Recrystallization solvent: Ethyl acetate

Melting Point: 234 - 236°C

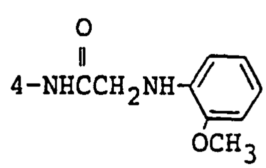
Form: Free

Example 295

Structure



R^2: H

R^3: 

Crystalline form: Colorless scales

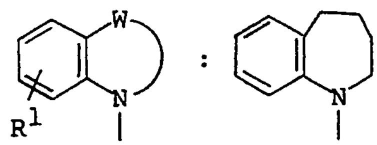
Recrystallization solvent: Ethyl acetate

Melting Point: 172 - 174°C

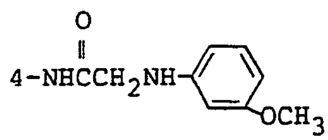
Form: Free

Example 296

Structure



R^2: H

R^3: 

Crystalline form: White powder

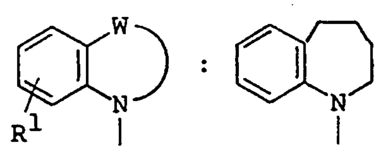
Recrystallization solvent: Ethyl acetate

Melting Point: 154 - 155°C

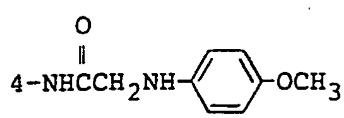
Form: Free

Example 297

Structure



R^2: H

R^3: 

Crystalline form: Light yellow needles

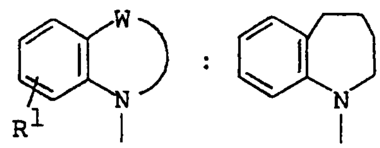
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 181.5 - 183.5°C

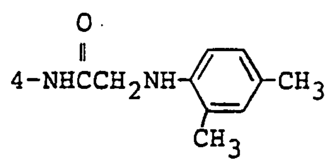
Form: Free

Example 298

Structure



R^2: H

R^3: 

Crystalline form: White powder

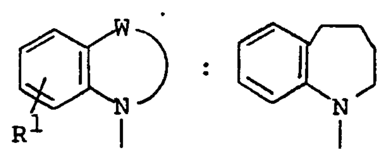
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 173 - 175°C

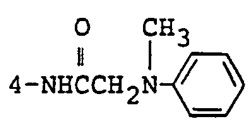
Form: Free

Example 299

Structure



R^2: H

R^3: 

Crystalline form: White powder

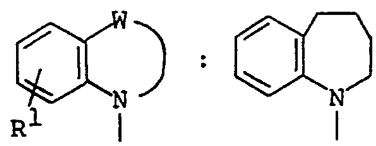
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 137 - 138°C

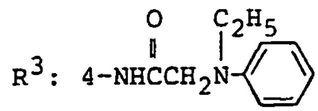
Form: Free

Example 300

Structure



R^2: H



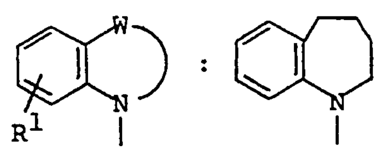
Crystalline form: Light yellow amorphous

NMR analysis: 42)

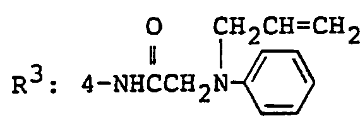
Form: Free

Example 301

Structure



R^2: H



Crystalline form: Colorless needles

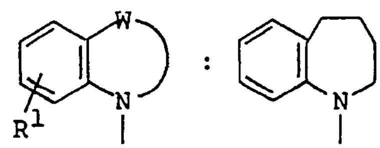
Recrystallization solvent: Diethyl ether/ethyl acetate

Melting Point: 129 - 130°C

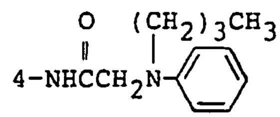
Form: Free

Example 302

Structure



R^2: H

R^3: 

Crystalline form: Colorless needles

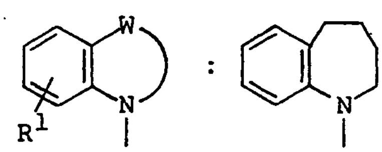
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 181 - 183°C

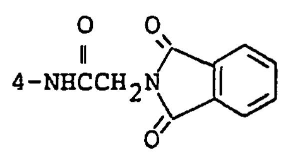
Form: Free

Example 303

Structure



R^2: H

R^3: 

Crystalline form: White powder

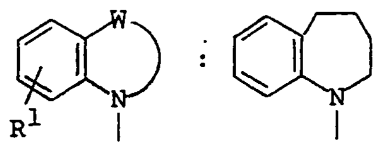
Recrystallization solvent: Ethyl acetate

Melting Point: 248 - 249°C

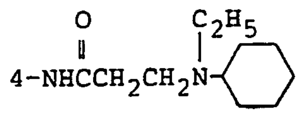
Form: Free

Example 304

Structure



R^2: H

R^3: 

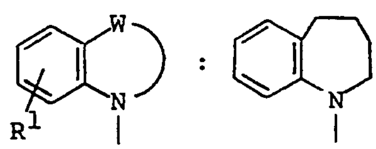
Crystalline form: Light yellow amorphous

NMR analysis: 43)

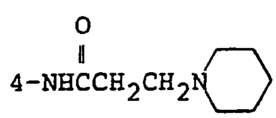
Form: Free

Example 305

Structure



R^2: H

R^3: 

Crystalline form: Light yellow needles

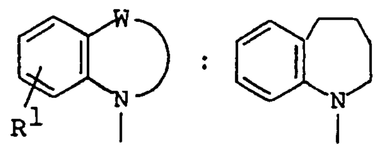
Recrystallization solvent: Ethanol

Melting Point: 94 - 96°C

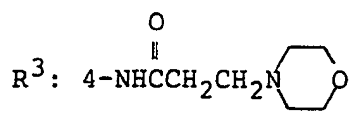
Form: Free

Example 306

Structure



R^2: H



Crystalline form: Light brown powder

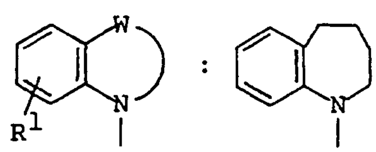
Recrystallization solvent: Ethyl acetate

Melting Point: 159 - 161°C

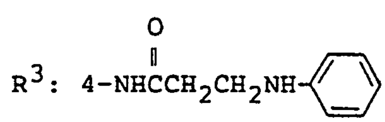
Form: Free

Example 307

Structure



R^2: H



Crystalline form: White powder

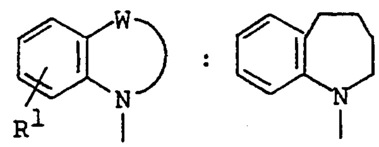
Recrystallization solvent: Ethyl acetate

Melting Point: 180 - 183°C

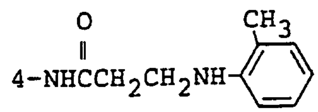
Form: Free

Example 308

Structure



R^2: H

R^3: 

Crystalline form: Light brown powder

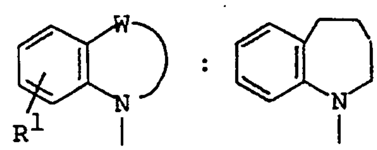
Recrystallization solvent: Ethanol

Melting Point: 177 - 180°C

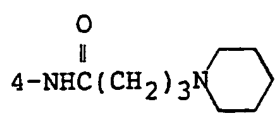
Form: Free

Example 309

Structure



R^2: H

R^3: 

Crystalline form: White powder

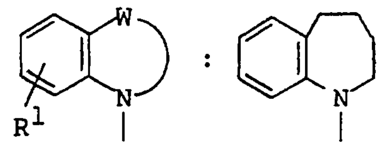
Recrystallization solvent: Ethyl acetate

Melting Point: 91 - 93°C

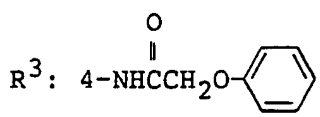
Form: Free

Example 310

Structure



R^2: H



Crystalline form: Light brown scales

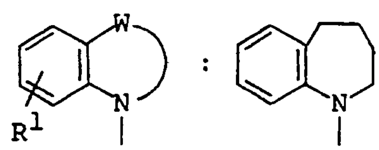
Recrystallization solvent: Ethanol

Melting Point: 155 - 156.5°C

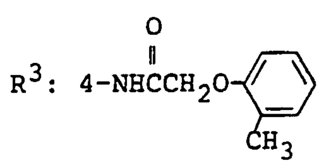
Form: Free

Example 311

Structure



R^2: H



Crystalline form: Colorless scales

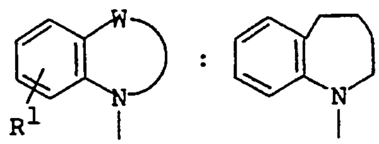
Recrystallization solvent: Ethyl acetate

Melting Point: 172.5 - 175°C

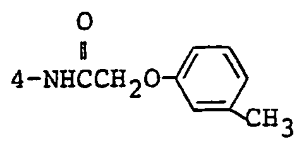
Form: Free

Example 312

Structure



R^2: H

R^3: 

Crystalline form: White powder

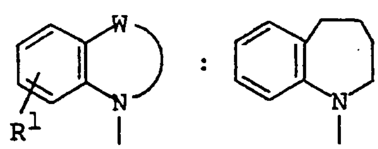
Recrystallization solvent: Ethanol

Melting Point: 148 - 150.5°C

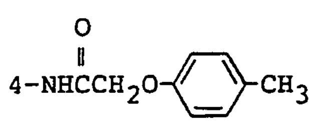
Form: Free

Example 313

Structure



R^2: H

R^3: 

Crystalline form: White powder

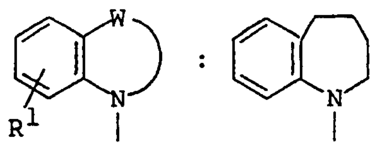
Recrystallization solvent: Ethyl acetate

Melting Point: 172 - 173°C

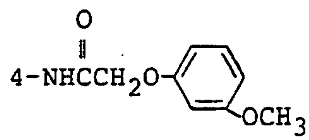
Form: Free

Example 314

Structure



R^2: H

R^3: 

Crystalline form: Colorless scales

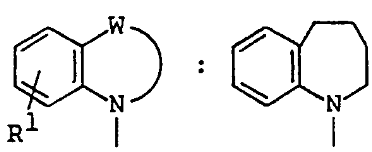
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 133 - 135°C

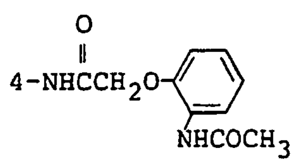
Form: Free

Example 315

Structure



R^2: H

R^3: 

Crystalline form: White powder

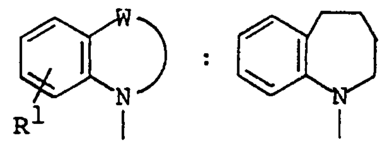
Recrystallization solvent: Ethyl acetate

Melting Point: 217 - 219°C

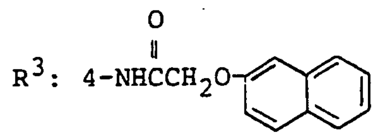
Form: Free

Example 316

Structure



R^2: H



Crystalline form: Colorless needles

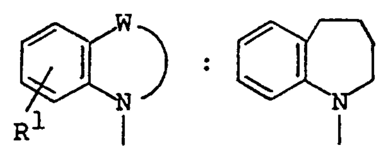
Recrystallization solvent: Ethyl acetate

Melting Point: 226 - 227.5°C

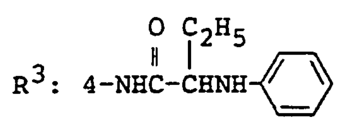
Form: Free

Example 317

Structure



R^2: H



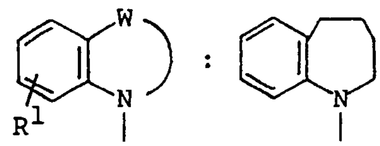
Crystalline form: Colorless amorphous

NMR analysis: 44)

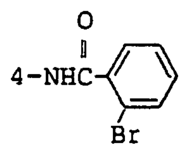
Form: Free

Example 318

Structure



R^2: H

R^3: 

Crystalline form: White powder

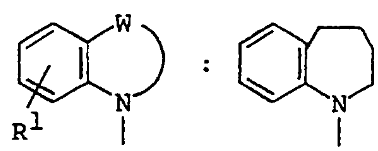
Recrystallization solvent: Dichloromethane

Melting Point: 234 - 235°C

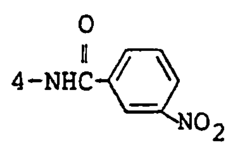
Form: Free

Example 319

Structure



R^2: H

R^3: 

Crystalline form: Colorless prisms

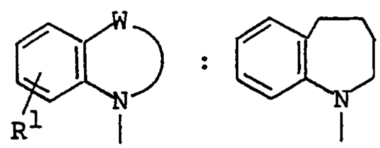
Recrystallization solvent: Methanol

Melting Point: 218 - 218.5°C

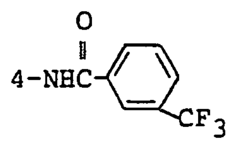
Form: Free

Example 320

Structure



R^2: H

R^3: 

Crystalline form: Colorless prisms

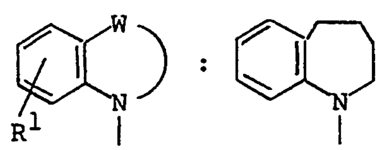
Recrystallization solvent: Ethanol

Melting Point: 202.5 - 206°C

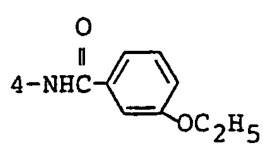
Form: Free

Example 321

Structure



R^2: H

R^3: 

Crystalline form: White powder

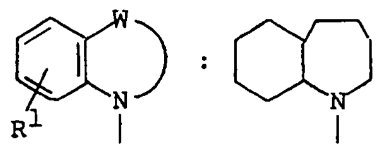
Recrystallization solvent: Ethanol

Melting Point: 174 - 176°C

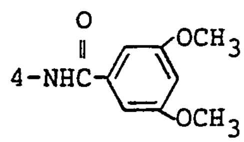
Form: Free

Example 322

Structure



R^2: H

R^3: 

Crystalline form: Colorless prisms

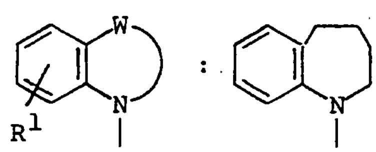
Recrystallization solvent: Ethanol

Melting Point: 216 - 218°C

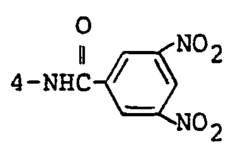
Form: Free

Example 323

Structure



R^2: H

R^3: 

Crystalline form: White powder

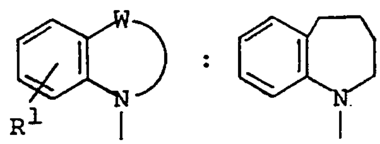
Melting Point: >300°C

NMR analysis: 45)

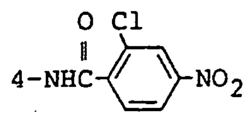
Form: Free

Example 324

Structure



R^2: H

R^3: 

Crystalline form: Colorless prisms

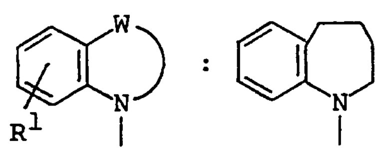
Recrystallization solvent: Ethanol

Melting Point: 250.5 - 251°C

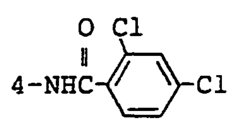
Form: Free

Example 325

Structure



R^2: H

R^3: 

Crystalline form: Colorless prisms

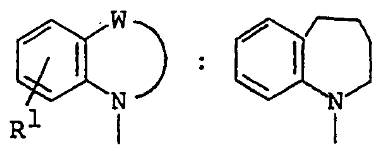
Recrystallization solvent: Ethanol

Melting Point: 223 - 225°C

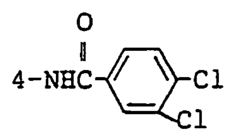
Form: Free

Example 326

Structure



R^2: H

R^3: 

Crystalline form: Colorless prismsr

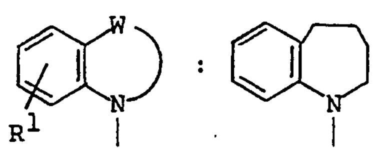
Recrystallization solvent: Methanol

Melting Point: 213 - 214°C

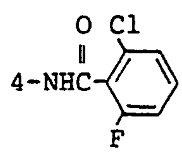
Form: Free

Example 327

Structure



R^2: H

R^3: 

Crystalline form: Colorless prisms

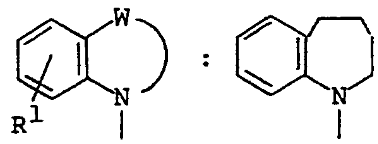
Recrystallization solvent: Ethanol

Melting Point: 246 - 247°C

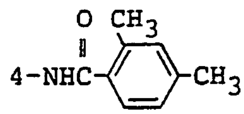
Form: Free

Example 328

Structure



R^2: H

R^3: 

Crystalline form: Colorless prisms

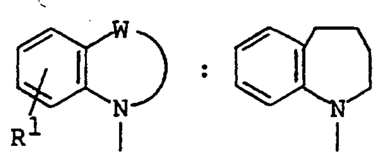
Recrystallization solvent: Methanol

Melting Point: 248 - 251°C

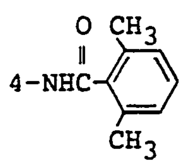
Form: Free

Example 329

Structure



R^2: H

R^3: 

Crystalline form: Colorless prisms

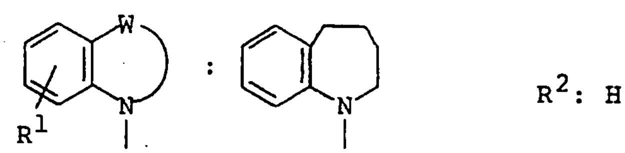
Recrystallization solvent: Ethanol

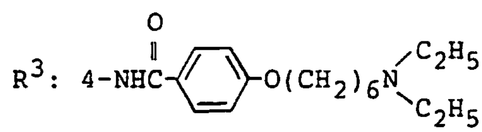
Melting Point: 268.5 - 270.5°C

Form: Free

Example 330

Structure





Crystalline form: White powder

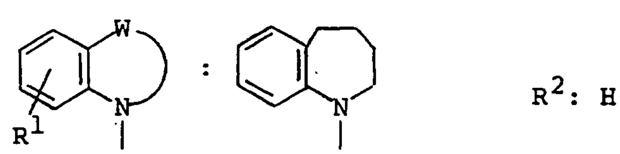
Recrystallization solvent: Methanol/diethyl ether

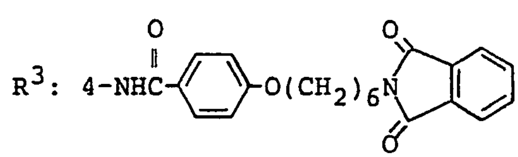
Melting Point: 174 - 176°C

Form: Hydrochloride

Example 331

Structure





Crystalline form: White powder

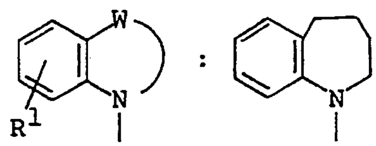
Recrystallization solvent: Ethanol

Melting Point: 130 - 134°C

Form: Free

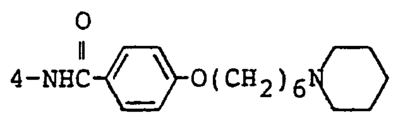
Example 332

Structure



R^2: H

R^3:



Crystalline form: White powder

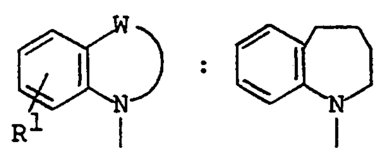
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 214 - 217°C

Form: Hydrochloride

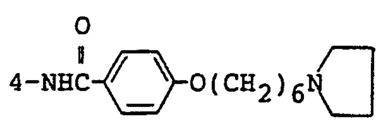
Example 333

Structure



R^2: H

R^3:



Crystalline form: White powder

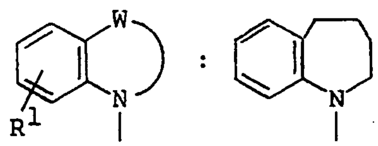
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 218 - 220°C

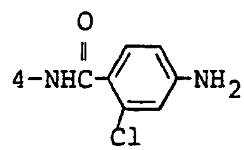
Form: Hydrochloride

Example 334

Structure



R^2: H

R^3: 

Crystalline form: White powder

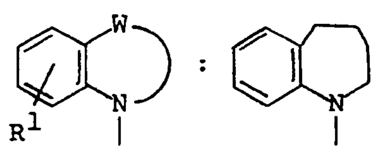
Recrystallization solvent: Ethyl acetate

Melting Point: 222 - 225°C

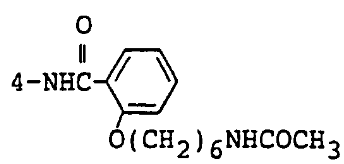
Form: Free

Example 335

Structure



R^2: H

R^3: 

Crystalline form: Colorless needles

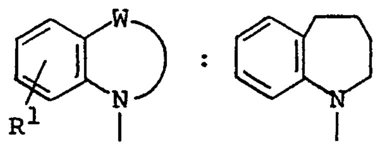
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 171 - 172°C

Form: Free

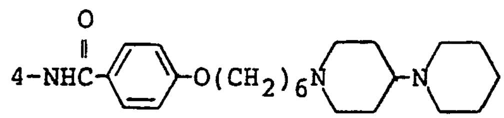
Example 336

Structure



R^2: H

R^3:



Crystalline form: White powder

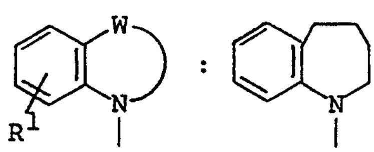
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 235.5 - 236°C

Form: Dihydrochloride

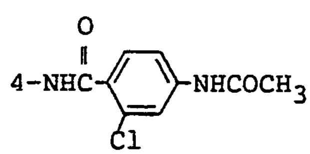
Example 337

Structure



R^2: H

R^3:



Crystalline form: White powder

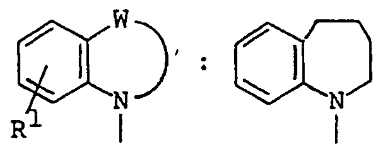
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 241 - 243°C

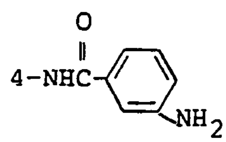
Form: Free

Example 338

Structure



R^2: H

R^3: 

Crystalline form: White powder

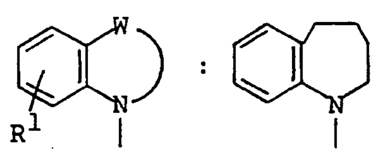
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 187 - 191°C

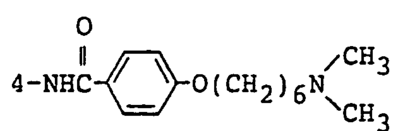
Form: Free

Example 339

Structure



R^2: H

R^3: 

Crystalline form: White powder

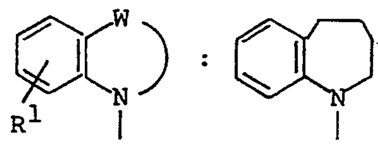
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 240 - 244°C

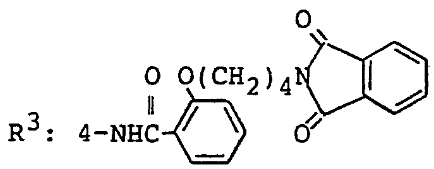
Form: Hydrochloride

Example 340

Structure



R^2: H



Crystalline form: Colorless prisms

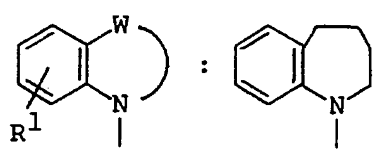
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 181 - 182°C

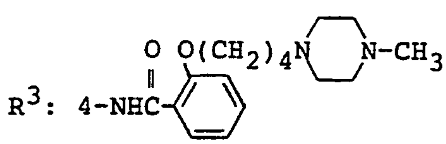
Form: Free

Example 341

Structure



R^2: H



Crystalline form: Colorless prisms

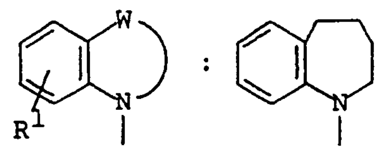
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 188 - 190°C

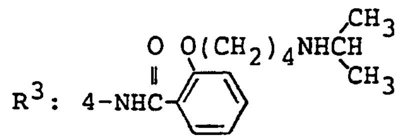
Form: Dihydrochloride

Example 342

Structure



R^2: H



Crystalline form: White powder

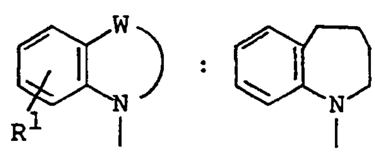
Recrystallization solvent: Isopropyl alcohol

Melting Point: 218 - 218.5°C

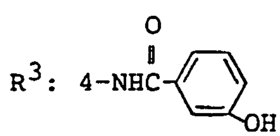
Form: Hydrochloride

Example 343

Structure



R^2: H



Crystalline form: White powder

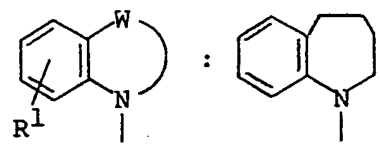
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 243 - 245.5°C

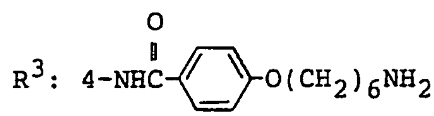
Form: Free

Example 344

Structure



R^2: H



Crystalline form: White powder

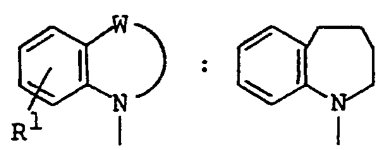
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 130 - 133°C

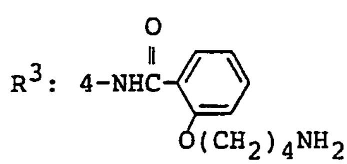
Form: Free

Example 345

Structure



R^2: H



Crystalline form: White powder

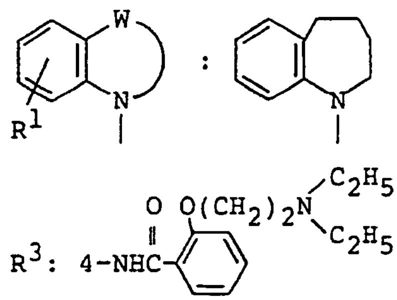
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 155 - 158°C

Form: Free

Example 346

Structure



R^2: H

Crystalline form: White powder

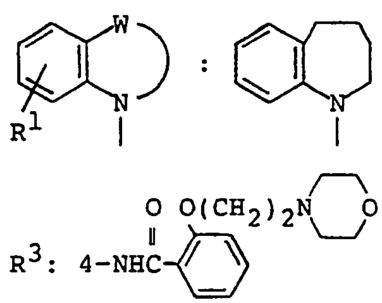
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 208 - 210°C

Form: Hydrochloride

Example 347

Structure



R^2: H

Crystalline form: Colorless prisms

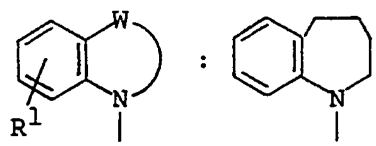
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 154 - 155°C

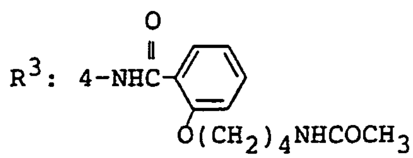
Form: Hydrochloride

Example 348

Structure



R^2: H



Crystalline form: White powder

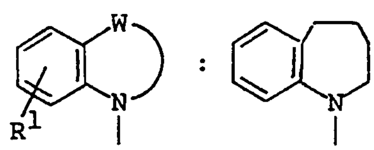
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 142 - 143°C

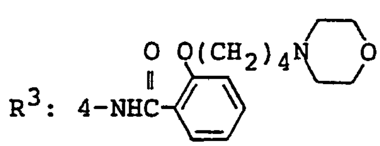
Form: Free

Example 349

Structure



R^2: H



Crystalline form: White powder

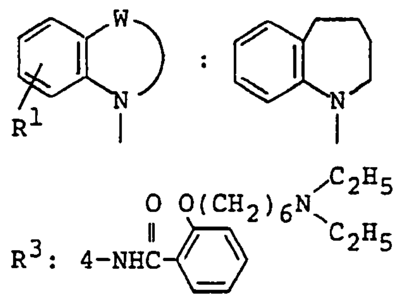
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 120 - 125°C

Form: Hydrochloride

Example 350

Structure



R^2: H

Crystalline form: White powder

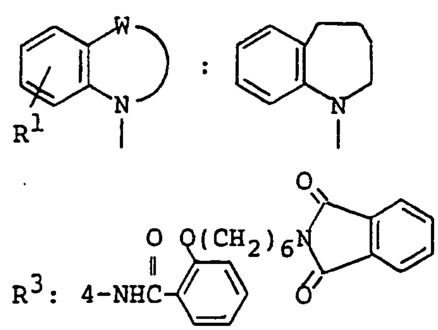
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 91 - 95°C

Form: Hydrochloride

Example 351

Structure



R^2: H

Crystalline form: White powder

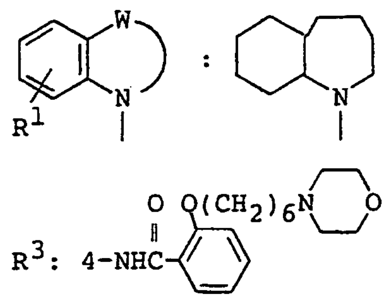
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 145 - 146.5°C

Form: Free

Example 352

Structure



R^2: H

Crystalline form: White powder

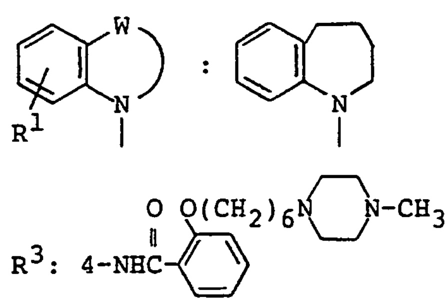
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 105 - 105.5°C

Form: Free

Example 353

Structure



R^2: H

Crystalline form: White powder

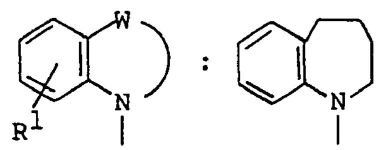
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 151 - 155°C

Form: Dihydrochloride

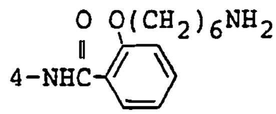
Example 354

Structure



R^2: H

R^3:



Crystalline form: White powder

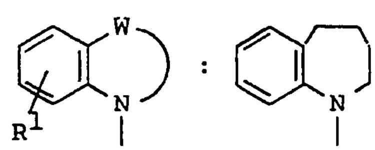
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 135.5 - 137.5°C

Form: Free

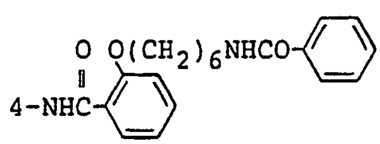
Example 355

Structure



R^2: H

R^3:



Crystalline form: White powder

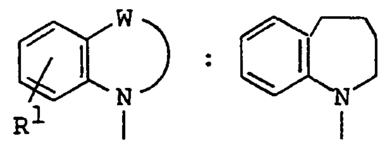
Recrystallization solvent: Ethanol

Melting Point: 178 - 178.5°C

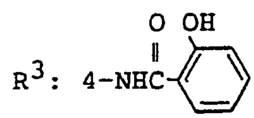
Form: Free

Example 356

Structure



R^2: H



Crystalline form: White powder

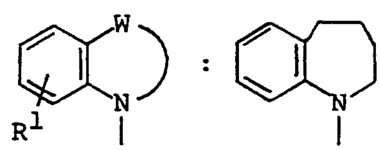
Recrystallization solvent: Dichloromethane

Melting Point: 266.5 - 268°C

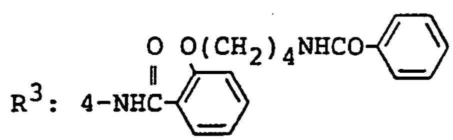
Form: Free

Example 357

Structure



R^2: H



Crystalline form: White powder

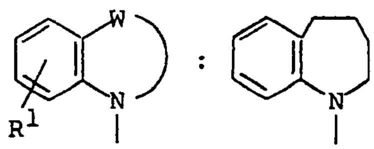
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 123 - 124°C

Form: Free

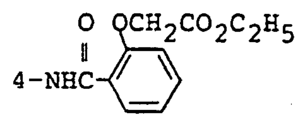
Example 358

Structure



R^2: H

R^3:



Crystalline form: White powder

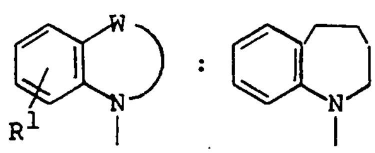
Recrystallization solvent: Ethyl acetate

Melting Point: 212 - 213.5°C

Form: Free

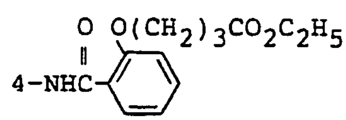
Example 359

Structure



R^2: H

R^3:



Crystalline form: Colorless scales

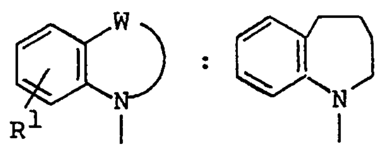
Recrystallization solvent: Ethyl acetate

Melting Point: 160.5 - 162°C

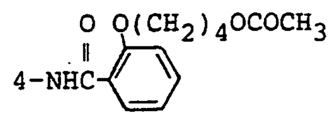
Form: Free

Example 360

Structure



R^2: H

R^3: 

Crystalline form: Colorless needles

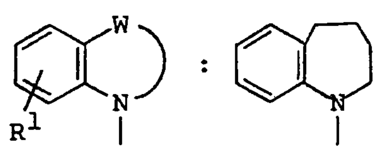
Recrystallization solvent: Ethanol

Melting Point: 103 - 105°C

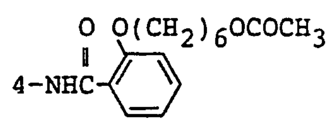
Form: Free

Example 361

Structure



R^2: H

R^3: 

Crystalline form: White powder

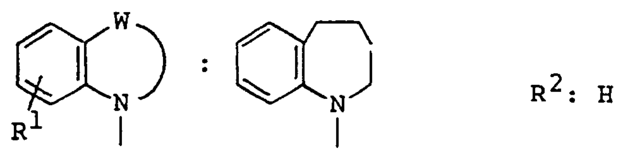
Recrystallization solvent: Ethanol

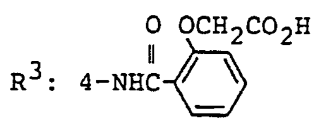
Melting Point: 145 - 146°C

Form: Free

Example 362

Structure





Crystalline form: White powder

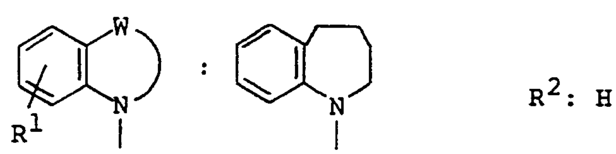
Recrystallization solvent: Methanol/diethyl ether

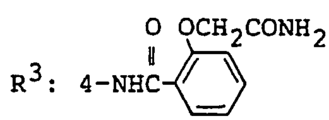
Melting Point: 247 - 250°C

Form: Free

Example 363

Structure





Crystalline form: White powder

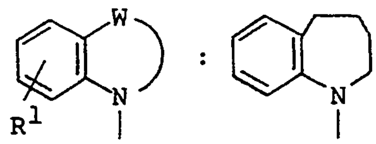
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 198 - 199°C

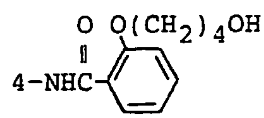
Form: Free

Example 364

Structure



R^2: H

R^3: 

Crystalline form: White powder

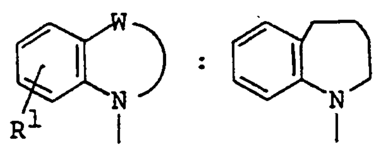
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 181.5 - 182.5°C

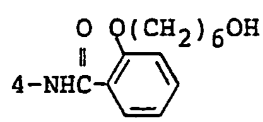
Form: Free

Example 365

Structure



R^2: H

R^3: 

Crystalline form: White powder

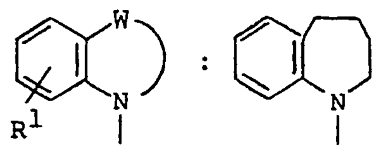
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 170 - 170.5°C

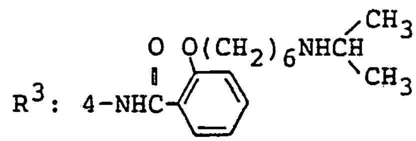
Form: Free

Example 366

Structure



R^2: H



Crystalline form: White powder

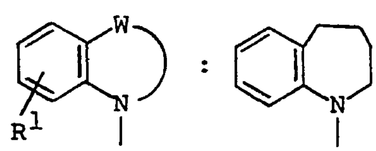
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 156 - 158°C

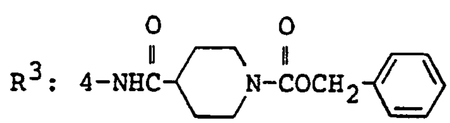
Form: Hydrochloride

Example 367

Structure



R^2: H



Crystalline form: White powder

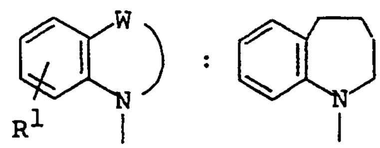
Recrystallization solvent: Diethyl ether

Melting Point: 168.5 - 170.5°C

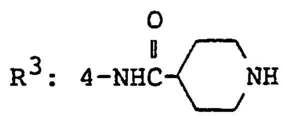
Form: Free

Example 368

Structure



R^2: H



Crystalline form: White powder

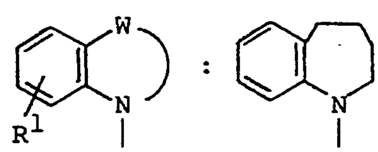
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 177 - 181.5°C

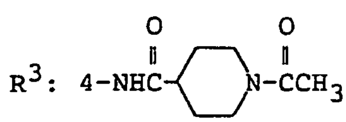
Form: Hydrochloride

Example 369

Structure



R^2: H



Crystalline form: White powder

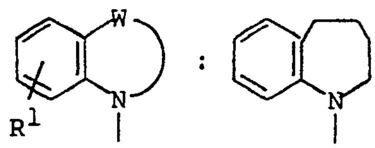
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 211 - 213°C

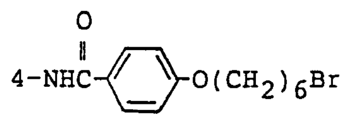
Form: Free

Example 370

Structure



R^2: H

R^3: 

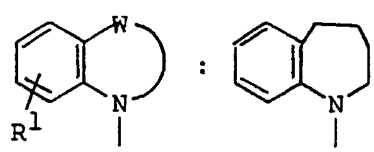
Crystalline form: White powder

NMR analysis: 46)

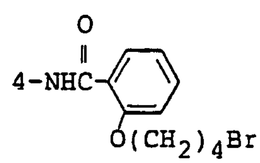
Form: Free

Example 371

Structure



R^2: H

R^3: 

Crystalline form: White powder

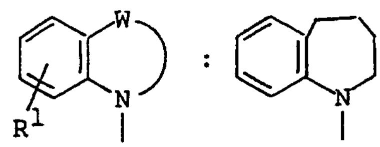
Recrystallization solvent: Methanol/ethyl acetate

Melting Point: 166 - 167°C

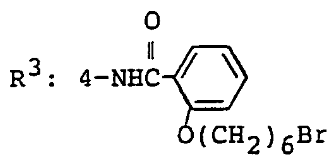
Form: Free

Example 372

Structure



R^2: H



Crystalline form: White powder

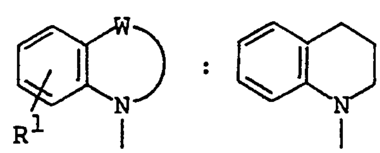
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 127 - 131°C

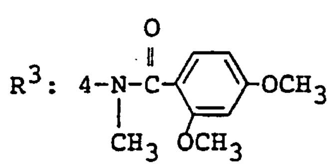
Form: Free

Example 373

Structure



R^2: H



Crystalline form: White powder

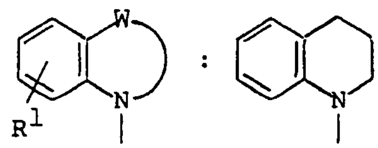
Recrystallization solvent: Methanol

Melting Point: 170 - 171°C

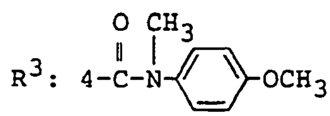
Form: Free

Example 374

Structure



R^2: H



Crystalline form: White powder

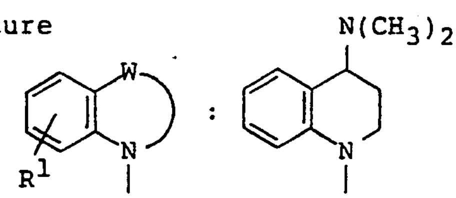
Recrystallization solvent: Methanol

Melting Point: 125 - 126°C

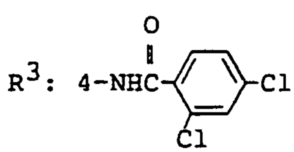
Form: Free

Example 375

Structure



R^2: H



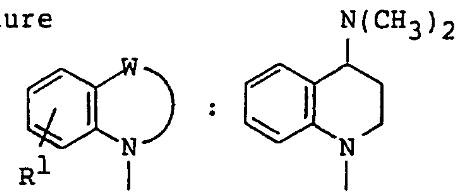
Crystalline form: Light yellow amorphous

NMR analysis: 47)

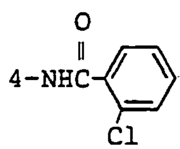
Form: Hydrochloride

Example 376

Structure



R^2: H

R^3: 

Crystalline form: Colorless amorphous

NMR analysis: 48)

Form: Hydrochloride

1) ^{1}H-NMR ($CDCl_3$) δ : 1.92 (1H, t, J=6.2 Hz), 1.98 (1H, t, J=6.4 Hz), 2.8 (2H, t, J=6.4 Hz), 3.76 (2H, t, J=6.2 Hz), 6.75 (1H, d, J=7.6 Hz), 6.86 (2H, d, J=8.6 Hz), 6.8-7.1 (2H, m), 7.20 (1H, d, J=7 Hz), 7.30 (2H, d, J=8.6 Hz), 7.72 (2H, d, J=8.6 Hz), 7.84 (2H, d, J=8.6 Hz), 10.13 (1H, s)

2) ^{1}H-NMR (DMSO-d_6) δ : 2.05 (2H, quint, J=6.4 Hz), 2.91 (2H, t, J=6.4 Hz), 3.86 (2H, t, J=6.4 Hz), 6.85 (1H, d, J=7.6 Hz), 6.9-7.2 (2H, m), 7.30 (1H, d, J=7.2 Hz), 7.44 (2H, d, J=8.5 Hz), 7.85 (2H, d, J=8.5 Hz), 8.1-8.2 (4H, m), 10.65 (1H, s), 13.2-13.4 (1H, br)

3) ^{1}H-NMR ($CDCl_3$) δ : 1.9-2.1 (2H, m), 2.84 (2H, t, J=6.5 Hz), 3.82 (6H, s), 3.90 (2H, t, J=6.6 Hz), 6.5-7.2 (7H, m), 7.35 (2H, d, J=8.7 Hz), 7.55 (2H, d, J=8.7 Hz), 8.05 (1H, s)

4) ^{1}H-NMR ($CDCl_3$) δ : 1.9-2.1 (2H, m), 2.37 (6H, s), 2.84 (2H, t, J=6.6 Hz), 3.90 (2H, t, J=6.6 Hz), 6.71 (1H, d, J=7.9 Hz), 6.8-7.2 (4H, m), 7.35 (2H, d, J=8.6 Hz), 7.44 (2H, s), 7.56 (2H, d, J=8.6 Hz), 8.00 (1H, s)

5) ^{1}H-NMR ($CDCl_3$) δ : 1.9-2.2 (2H, m), 2.12 (3H, s), 2.84 (2H, t, J=6.6 Hz), 3.89 (2H, t, J=6.5 Hz), 6.71 (1H, d, J=7.8 Hz), 6.87 (1H, t, J=7 Hz), 6.99 (1H, t, J=7.3 Hz), 7.15 (1H, d, J=6.5 Hz), 7.28 (2H, d, J=8.6 Hz), 7.41 (2H, d, J=8.6 Hz), 8.03

(1H, s)

6) ^{1}H-NMR ($CDCl_3$) δ : 0.8-1.3 (6H, m), 1.6-2.3 (9H, m), 2.83 (2H, t, J=6.6 Hz), 3.89 (2H, t, J=6.5 Hz), 6.72 (1H, d, J=7.9 Hz), 6.8-7.1 (2H, m), 7.15 (1H, d, J=7.4 Hz), 7.28 (2H, d, J=8.3 Hz), 7.44 (2H, d, J=8.4 Hz), 7.9-8.1 (1H, m)

7) ^{1}H-NMR ($CDCl_3$) δ : 2.02 (2H, quint, J=6.5 Hz), 2.81 (2H, t, J=6.6 Hz), 3.69 (2H, s), 3.87 (2H, t, J=6.6 Hz), 6.66 (1H, d, J=8.2 Hz), 6.8-7.0 (2H, m), 7.13 (1H, d, J=7.3 Hz), 7.2-7.4 (9H, m), 7.59 (1H, s)

8) ^{1}H-NMR ($CDCl_3$) δ : 1.7-2.1 (17H, m), 2.83 (2H, t, J=6.7 Hz), 3.90 (2H, t, J=6.6 Hz), 6.68 (1H, d, J=8.1 Hz), 6.8-7.1 (2H, m), 7.14 (1H, d, J=7 Hz), 7.32 (2H, d, J=8.7 Hz), 7.39 (1H, s), 7.46 (2H, d, J=8.7 Hz)

9) ^{1}H-NMR ($CDCl_3$) δ : 1.99 (2H, quint, J=6.5 Hz), 2.82 (2H, t, J=6.6 Hz), 3.82 (2H, t, J=6.5 Hz), 6.8-7.1 (4H, m), 7.1-7.3 (2H, m), 7.4-7.6 (3H, m), 7.67 (1H, s), 7.8-8.0 (3H, m), 8.42 (1H, s)

10) ^{1}H-NMR ($CDCl_3$) δ : 2.00 (2H, quint, J=6.5 Hz), 2.83 (2H, t, J=6.6 Hz), 3.85 (2H, t, J=6.6 Hz), 3.86 (3H, s), 6.8-7.1 (6H, m), 7.1-7.3 (2H, m), 7.64 (1H, s), 7.8-8.0 (3H, m), 8.22 (1H, s)

11) ^{1}H-NMR ($CDCl_3$) δ : 1.98 (2H, quint, J=6.5 Hz), 2.82 (2H, t, J=6.5 Hz), 3.81 (2H, t, J=6.5 Hz),

3.84 (3H, s), 6.8-7.5 (10H, m), 7.68 (1H, s), 7.95 (1H, d, J=8.2 Hz), 8.52 (1H, s)

12) ^{1}H-NMR ($CDCl_3$) δ : 1.7-1.9 (2H, m), 2.70 (2H, t, J=6.6 Hz), 3.70 (2H, t, J=6.4 Hz), 6.8-7.3 (6H, m), 7.4-7.7 (2H, m), 7.8-7.9 (5H, m), 8.04 (1H, d, J=8 Hz), 8.33 (1H, s), 8.90 (1H, s)

13) ^{1}H-NMR ($CDCl_3$) δ : 1.7-2.1 (17H, m), 2.84 (2H, t, J=6.5 Hz), 3.89 (2H, t, J=6.4 Hz), 6.8-7.2 (6H, m), 7.42 (1H, s), 7.56 (1H, s), 7.81 (1H, d, J=8.1 Hz)

14) ^{1}H-NMR (DMSO-d_6) δ : 1.0-1.5 (5H, m), 1.5-2.0 (5H, m), 2.2-3.8 (8H, m), 4.2-5.2 (3H, m), 6.77 (1H, d, J=7.2 Hz), 7.1-7.4 (4H, m), 7.47 (2H, d, J=8.6 Hz), 7.58 (1H, d, J=6.2 Hz), 10.06 (1H, s), 10.9-12.1 (1H, br)

15) ^{1}H-NMR (DMSO-d_6) δ : 2.5-3.8 (6H, m), 4.2-5.2 (3H, m), 6.81 (1H, d, J=6.8 Hz), 7.1-7.3 (4H, m), 7.5-7.7 (3H, m), 7.8-8.0 (1H, m), 7.97 (2H, d, J=1.8 Hz), 10.66 (1H, s), 11.1-12.3 (1H, br)

16) ^{1}H-NMR (DMSO-d_6) δ : 2.20 (3H, s), 2.27 (3H, s), 2.5-3.8 (6H, m), 4.3-5.3 (3H, m), 6.82 (1H, d, J=7.2 Hz), 7.1-7.4 (7H, m), 7.5-7.8 (3H, m), 10.43 (1H, s), 11.0-12.2 (1H, br)

17) ^{1}H-NMR (DMCO-d_6) δ : 2.34 (3H, s), 2.5-3.7 (6H, m), 4.3-5.2 (3H, m), 6.82 (1H, d, J=6.8 Hz), 7.2-7.7 (11H, m), 10.41 (1H, s), 10.8-12.3 (1H, br)

18) ^{1}H-NMR (DMSO-d_6) δ : 2.38 (3H, s), 2.5-3.8 (6H, m),

4.3-5.3 (3H, m), 6.81 (1H, d, J=7.0 Hz), 7.1-7.5 (6H, m), 7.5-7.8 (5H, m), 10.35 (1H, s), 10.9-12.2 (1H, br)

19) ^{1}H-NMR (DMSO-d_6) δ : 2.37 (3H, s), 2.5-3.7 (6H, m), 4.3-5.2 (3H, m), 6.81 (1H, d, J=7.2 Hz), 7.2-7.4 (6H, m), 7.5-7.7 (3H, m), 7.84 (2H, d, J=8.0 Hz), 10.31 (1H, s), 10.9-12.2 (1H, br)

20) ^{1}H-NMR (DMSO-d_6) δ : 2.5-3.8 (6H, m), 4.3-5.2 (3H, m), 6.82 (1H, d, J=7.4 Hz), 7.2-7.3 (4H, m), 7.5-7.8 (5H, m), 7.75 (1H, d, J=1.8 Hz), 10.70 (1H, s), 10.8-12.2 (1H, br)

21) ^{1}H-NMR (DMSO-d_6) δ : 2.5-3.8 (9H, m), 4.3-4.7 (1H, m), 4.7-5.1 (2H, m), 6.8-7.1 (3H, m), 7.1-7.4 (2H, m), 7.5-7.7 (2H, m), 7.8-8.0 (3H, m), 9.79 (1H, s), 10.8-12.2 (1H, br)

22) ^{1}H-NMR (DMSO-d_6) δ : 0.8-1.2 (3H, m), 1.7-2.2 (2H, m), 2.5-3.8 (5H, m), 4.3-5.2 (3H, m), 6.80 (1H, d, J=7.2 Hz), 7.1-7.3 (4H, m), 7.6-7.7 (3H, m), 7.85 (1H, s), 7.96 (2H, d, J=1.8 Hz), 10.62 (1H, s), 10.8-12.0 (1H, br)

23) ^{1}H-NMR (DMSO-d_6) δ : 0.8-1.1 (3H, m), 1.7-2.1 (2H, m), 2.37 (3H, s), 2.7-3.8 (5H, m), 4.4-5.2 (3H, m), 6.81 (1H, d, J=7.6 Hz), 7.2-7.4 (6H, m), 7.6-7.7 (3H, m), 7.84 (2H, d, J=8.2 Hz), 10.29 (1H, s), 10.5-11.8 (1H, br)

24) ^{1}H-NMR (DMSO-d_6) δ : 0.8-1.2 (3H, m), 1.7-2.1 (2H,

m), 2.38 (3H, s), 2.6-3.8 (5H, m), 4.3-5.2 (3H, m), 6.81 (1H, d, J=7.0 Hz), 7.2-7.5 (6H, m), 7.6-7.8 (5H, m), 10.33 (1H, s), 10.5-11.7 (1H, br)

25) ^{1}H-NMR (DMSO-d_6) δ : 0.8-1.2 (3H, m), 1.7-2.1 (2H, m), 2.6-3.8 (5H, m), 3.8-5.2 (3H, m), 6.82 (1H, d, J=7.2 Hz), 7.1-7.5 (8H, m), 7.5-7.7 (3H, m), 10.42 (1H, s), 10.7-12.0 (1H, br)

26) ^{1}H-NMR (DMSO-d_6) δ : 0.8-2.0 (15H, m), 2.2-2.5 (1H, m), 2.6-3.7 (5H, m), 4.3-5.2 (3H, m), 6.76 (1H, d, J=7.0 Hz), 7.1-7.4 (4H, m), 7.46 (2H, d, J=8.6 Hz), 7.61 (1H, d, J=6.4 Hz), 10.03 (1H, s), 10.5-11.8 (1H, br)

27) ^{1}H-NMR (DMSO-d_6) δ : 0.8-1.1 (3H, m), 1.7-2.0 (2H, m), 2.20 (3H, s), 2.29 (3H, s), 2.6-3.7 (5H, m), 4.3-5.2 (3H, m), 6.82 (1H, d, J=7.0 Hz), 7.2-7.4 (7H, m), 7.5-7.7 (3H, m), 10.41 (1H, s), 10.6-12.0 (1H, br)

28) ^{1}H-NMR ($CDCl_3$) δ : 1.21 (3H, t, J=7.1 Hz), 3.00-3.25 (3H, m), 4.00-4.30 (4H, m), 6.63 (1H, d, J=7.8 Hz), 6.86 (1H, t, J=7.3 Hz), 7.00 (1H, t, J=6.3 Hz), 7.10-7.31 (3H, m), 7.40-7.57 (3H, m), 7.77 (2H, d, J=1.9 Hz), 8.76 (1H, brs)

29) ^{1}H-NMR ($CDCl_3$) δ : 2.29 (3H, s), 2.32 (3H, s), 2.34 (3H, s), 2.50-3.15 (11H, m), 3.79 (1H, dd, J=13.2 Hz, 7.3 Hz), 4.05 (1H, dd, J=13.2 Hz, 5.7 Hz), 6.62 (1H, d, J=7.7 Hz), 6.82-7.48 (8H, m), 7.53 (2H, d,

J=8.4 Hz), 8.05 (1H, brs)

30) ^{1}H-NMR ($CDCl_3$) δ : 1.65-2.01 (4H, m), 2.31 (3H, s), 2.35 (3H, s), 2.55-3.02 (6H, m), 3.09 (1H, dd, J=15 Hz, 5 Hz), 3.70 (1H, dd, J=12.5 Hz, 8.0 Hz), 4.22 (1H, dd, J=12.5 Hz, 5 Hz), 6.67 (1H, d, J=7.8 Hz), 6.80-7.32 (7H, m), 7.37 (2H, d, J=8.6 Hz), 7.53 (1H, d, J=8.3 Hz), 7.66 (1H, brs)

31) ^{1}H-NMR ($CDCl_3$) δ : 2.80 (1H, dd, J=16.1 Hz, 5.3 Hz), 3.16 (1H, dd, J=15.8 Hz, 5.3 Hz), 3.75-4.50 (3H, m), 4.87-5.10 (3H, m), 6.80-7.60 (14H, m), 7.74 (2H, d, J=1.9 Hz), 8.47 (1H, brs)

32) ^{1}H-NMR ($CDCl_3$) δ : 2.35 (6H, s), 2.72-3.10 (3H, m), 3.65-3.78 (1H, m), 4.06-4.18 (1H, m), 6.60-7.62 (9H, m), 7.74 (2H, d, J=1.8 Hz), 8.52 (1H, brs)

33) ^{1}H-NMR ($CDCl_3$) δ : 1.87 (3H, s), 2.68 (1H, dd, J=5.6 Hz, 16 Hz), 3.14 (1H, dd, J=5.6 Hz, 16 Hz), 3.70-3.95 (2H, m), 4.32-4.50 (1H, m), 6.29 (1H, d, J=7.6 Hz), 6.90-7.80 (11H, m), 9.16 (1H, brs)

34) ^{1}H-NMR ($CDCl_3$) δ : 1.62 (1H, brs), 1.90-2.25 (2H, m), 2.55 (3H, s), 3.78 (1H, t, J=5.1 Hz), 3.95 (2H, t, J=6.7 Hz), 6.69 (1H, t, J=7.9 Hz), 6.90-7.13 (2H, m), 7.23-7.40 (3H, m), 7.42-7.56 (3H, m), 7.77 (2H, d, J=1.9 Hz), 8.53 (1H, brs)

35) ^{1}H-NMR ($CDCl_3$) δ : 1.80-2.02 (1H, m), 2.20-2.35 (1H, m), 2.31 (6H, s), 3.52 (1H, t, J=5.4 Hz), 3.68-3.83 (1H, m), 3.95-4.15 (1H, m), 6.59 (1H, d,

J=7.8 Hz), 6.81-7.10 (2H, m), 7.16-7.50 (6H, m), 7.80 (2H, d, J=1.8 Hz), 9.13 (1H, brs)

36) ^{1}H-NMR ($CDCl_3$) δ : 1.35-1.60 (1H, m), 1.65-2.20 (3H, m), 2.65-3.20 (5H, m), 3.81 (2H, d, J=6.5 Hz), 4.90-5.10 (1H, m), 6.60 (1H, d, J=8.0 Hz), 6.90 (1H, t, J=8.0 Hz), 7.00-7.50 (6H, m)

37) ^{1}H-NMR ($CDCl_3$) δ : 1.30-2.25 (4H, m), 2.55-3.20 (3H, m), 3.35 (2H, s), 3.80 (2H, s), 4.90-5.10 (1H, m), 6.62 (1H, d, J=8.0 Hz), 6.85-7.45 (12H, m), 9.27 (1H, brs)

38) ^{1}H-NMR ($CDCl_3$) δ : 1.35-2.25 (4H, m), 2.33 (3H, s), 2.60-3.20 (3H, m), 3.12 (2H, s), 3.61 (2H, s), 5.00 (1H, brs), 6.50-7.60 (13H, m), 9.14 (1H, brs)

39) ^{1}H-NMR ($CDCl_3$) δ : 1.27 (3H, t, J=7.1 Hz), 1.25-2.50 (12H, m), 2.70-3.10 (4H, m), 3.05 (2H, s), 4.15 (2H, q, J=7.0 Hz), 4.90-5.10 (1H, m), 6.63 (1H, d, J=7.5 Hz), 6.91 (1H, t, J=7.5 Hz), 7.00-7.50 (6H, m), 9.14 (1H, brs)

40) ^{1}H-NMR ($CDCl_3$) δ : 1.30-1.65 (1H, m), 1.80-2.25 (5H, m), 2.70-3.20 (3H, m), 4.01 (2H, d, J=5.0 Hz), 4.90-5.10 (1H, m), 6.61 (1H, d, J=7.7 Hz), 6.89 (1H, t, J=7.0 Hz), 7.00-7.45 (6H, m), 9.05 (1H, brs)

41) ^{1}H-NMR ($CDCl_3$) δ : 1.18 (6H, s), 1.30-2.20 (4H, m), 2.60-3.20 (3H, m), 3.30 (2H, s), 3.73 (2H, s), 4.90-5.10 (1H, m), 6.61 (1H, d, J=7.3 Hz), 6.70-

7.45 (12H, m), 9.50 (1H, brs)

42) ^{1}H-NMR ($CDCl_3$) δ : 1.19 (3H, t, J=7.0 Hz), 1.30-1.70 (1H, m), 1.75-2.20 (3H, m), 2.65-3.15 (3H, m), 3.46 (2H, q, J=7.0 Hz), 3.88 (2H, s), 4.90-5.10 (1H, m), 6.55-7.45 (13H, m), 8.36 (1H, brs)

43) ^{1}H-NMR ($CDCl_3$) δ : 1.08 (3H, t, J=7.2 Hz), 1.05-2.25 (14H, m), 2.25-3.25 (10H, m), 4.90-5.10 (1H, m), 6.64 (1H, d, J=7.6 Hz), 6.90 (1H, t, J=7.2 Hz), 6.94-7.50 (6H, m), 11.50 (1H, brs)

44) ^{1}H-NMR ($CDCl_3$) δ : 1.06 (3H, t, J=7.5 Hz), 1.30-2.20 (6H, m), 2.60-3.20 (3H, m), 3.65 (1H, m), 3.95 (1H, brs), 4.90-5.10 (1H, m), 6.50-6.75 (3H, m), 6.75-7.05 (2H, m), 7.05-7.55 (8H, m), 8.67 (1H, brs)

45) ^{1}H-NMR (DMSO-d_6) δ : 1.28-1.57 (1H, m), 1.69-2.20 (3H, m), 2.59-3.15 (3H, m), 4.74-4.98 (1H, m), 6.62-6.80 (1H, m), 6.86-7.37 (5H, m), 7.50-7.70 (2H, m), 8.95-9.02 (1H, m), 9.03-9.15 (2H, m), 10.85 (1H, s)

46) ^{1}H-NMR ($CDCl_3$) δ : 1.40-1.66 (5H, m), 1.72-2.20 (7H, m), 2.63-3.18 (3H, m), 3.42 (2H, t, J=6.7 Hz), 4.00 (2H, t, J=6.3 Hz), 4.91-5.13 (1H, m), 6.58-6.72 (1H, m), 6.82-7.00 (3H, m), 7.02-7.30 (4H, m), 7.36-7.51 (2H, m), 7.70-7.88 (2H, m), 7.91 (1H, s)

47) ^{1}H-NMR (DMSO-d_6) δ : 2.05-2.95 (8H, m), 3.43-3.70 (1H, m), 4.08-4.30 (1H, m), 4.72-5.00 (1H, m),

6.70-8.08 (11H, m), 10.8 (1H, s), 11.1 (1H, brs)

48) ^{1}H-NMR (DMSO-d_6) δ : 2.10-3.00 (8H, m), 3.47-3.70 (1H, m), 4.07-4.33 (1H, m), 4.75-4.98 (1H, m), 6.78-6.91 (1H, m), 7.05-7.22 (2H, m), 7.30-7.97 (9H, m), 10.75 (1H, s), 10.94 (1H, brs)

Example 377

To a solution of 1-[4-(4-formylbenzoylamino)-benzoyl]-1,2,3,4-tetrahydroquinoline (0.3 g) in methanol (10 ml) is added gradually sodium borohydride (59 mg) under ice-cooling and the mixture is stirred at room temperature for 2 hours. Water is added to the mixture and the solvent is distilled off under reduced pressure. The resulting residue is extracted with dichloromethane, washed with water, and dried over magnesium sulfate. The solvent is distilled off under reduced pressure and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane : methanol = 50 : 1), and recrystallized from methanol to give 1-[4-(4-hydroxymethylbenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (165 mg) as white powder, m.p. 224.5 - 225.5°C.

Using the suitable starting materials, the compound of the above Example 37 is obtained in the same manner as in Example 377.

Example 378

To a solution of 1-[4-(4-methoxycarbonylbenzoyl-

amino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.5 g) in methanol (20 ml) is added 5 % aqueous sodium hydroxide solution (10 ml) and the mixture is stirred at room temperature overnight. Methanol is distilled off under reduced pressure and the resulting residue is acidified with diluted aqueous hydrochloric acid solution. The precipitated crystal is collected by filtration to give 1-[4-(4-carboxybenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.4 g) as white powder, m.p. >300°C.

^{1}H-NMR (DMSO-d_6) δ : 2.05 (2H, quint, J=6.4 Hz), 2.91 (2H, t, J=6.4 Hz), 3.86 (2H, t, J=6.4 Hz), 6.85 (1H, d, J=7.6 Hz), 6.9-7.2 (2H, m), 7.30 (1H, d, J=7.2 Hz), 7.44 (2H, d, J=8.5 Hz), 7.85 (2H, d, J=8.5 Hz), 8.1-8.2 (4H, m), 10.65 (1H, s), 13.2-13.4 (1H, br)

Using the suitable starting materials, the compounds of the above Examples 39, 241, 252, 253 and 362 are obtained in the same manner as in Example 378.

Example 379

To a solution of 1-[4-(3-acetyloxybenzoylamino)-benzoyl]-1,2,3,4-tetrahydroquinoline (1.5 g) in methanol (20 ml) is added 5 % aqueous sodium hydroxide solution (10 ml) and the mixture is stirred at room temperature overnight. Methanol is distilled off under reduced pressure and the resulting residue is acidified with diluted aqueous hydrochloric acid solution. The precipitated crystal is collected by filtration and recrystallized from methanol to

give 1-[4-(3-hydroxybenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (1.22 g) as white powder, m.p. 217 - 218°C.

Using the suitable starting materials, the compounds of the above Examples 10, 343, 356, 364 and 365 are obtained in the same manner as in Example 379.

Example 380

To a solution of 1-[4-(3-hydroxybenzoylamino)-benzoyl]-1,2,3,4-tetrahydroquinoline (0.4 g) in acetone (5 ml) are added potassium carbonate (0.22 g) and ethyl iodide (0.34 g), and the mixture is refluxed for 5 hours. Then, acetone is distilled off under reduced pressure and water is added to the residue. The precipitated crystal is collected by filtration, and recrystallized from methanol to give 1-[4-(3-ethoxybenzoylamino)benzoyl]-1,2,3,4-tetrahydro-quinoline (0.36 g) as white powder, m.p. 170.5 - 171.5°C.

Using the suitable starting materials, the compounds of the above Examples 11, 12, 13, 14, 33, 35, 48, 50 - 55, 90 - 92, 97 - 100, 109 - 111, 120 - 122, 136 - 138, 165 - 167, 175 - 177, 192 - 194, 211, 212, 214, 321, 322, 330 - 333, 335, 336, 339 - 342, 344 - 355, 357 - 366 and 370 - 374 are obtained in the same manner as in Example 380.

Example 381

Ethanol (50 ml) is added to 10 % Pd-C (0.1 g) and thereto is added 1-[4-(3-nitrobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.73 g). The mixture is subjected to

catalytic reduction at ordinary temperature under atmospheric pressure of hydrogen. After completion of the reduction, 10 % Pd-C is removed by filtration and the filtrate is concentrated under reduced pressure. The residue is extracted with dichloromethane and the extract is dried over magnesium sulfate. The solvent is distilled off under reduced pressure and recrystallized from methanol to give 1-[4-(3-aminobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.54 g) as white powder, m.p. 205.5 - 206.5°C.

Using the suitable starting materials, the compounds of the above Examples 24, 334 and 338 are obtained in the same manner as in Example 381.

Example 382

To a solution of 1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline (0.5 g) in dichloromethane (20 ml) is added triethylamine (0.3 g), and thereto is added benzoyl chloride (0.28 g) under ice-cooling. The mixture is stirred at room temperature for 1 hour. To the reaction mixture is added water and extracted with dichloromethane. The extract is dried over magnesium sulfate and the solvent is distilled off under reduced pressure. The resulting residue is purified by silica gel column chromatography (eluent; dichloromethane : methanol = 50 : 1) and recrystallized from methanol to give 1-[4-(benzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (245 mg) as white powder, m.p. 202.5 - 203.5°C.

Using the suitable starting materials, the compounds of the above Examples 2 - 119, 131 - 373, 375 and 376 are obtained in the same manner as in Example 382.

Example 383

Thionyl chloride (10 ml) is added to 1-(4-carboxybenzoyl)-1,2,3,4-tetrahydroquinoline (0.5 g) and the mixture is refluxed for 1 hour. Thionyl chloride is distilled off under reduced pressure to give 4-[1-(1,2,3,4-tetrahydroquinolyl)carbonyl]benzoyl chloride. Separately, to a solution of m-anisidine (0.27 g) in dichloromethane (20 ml) is added triethylamine (0.34 g), and thereto is added gradually the above obtained 4-[1-(1,2,3,4-tetrahydroquinolyl)carbonyl]benzoyl chloride under ice-cooling and the mixture is stirred at room temperature for 1 hour. Water is added to the reaction mixture and the mixture is extracted with dichloromethane. The extract is dried over magnesium sulfate. The solvent is distilled off under reduced pressure and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane : methanol = 50 : 1), and recrystallized from methanol to give 1-[4-(3-methoxyanilinocarbonyl)benzoyl]-1,2,3,4-tetrahydroquinoline (203 mg) as colorless needles, m.p. 154 - 155°C.

Using the suitable starting materials, the compounds of the above Examples 120, 122 - 130 and 374 are obtained in the same manner as in Example 383.

Example 384

To 4-oxo-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.7 g) are added tetrahyrdofuran (10 ml) and methanol (10 ml). To the mixture is added sodium borohydride (0.1 g) in portions and the mixture is stirred at room temperature for 1 hour. Water is added to the reaction mixture and the mixture is extracted with dichloromethane. The solvent is concentrated and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane → dichloromethane : methanol = 20 : 1), and recrystallized from ethanol to give 4-hydroxy-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.4 g) as white powder, m.p. 215 - 217°C.

Example 385

To 3-ethoxycarbonyl-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.6 g) are added an aqueous solution of sodium hydroxide (0.1 g) in water (1 ml) and ethanol (5 ml). The mixture is stirred at room temperature for 15 minutes, and acidified with diluted hydrochloric acid, extracted with dichloromethane. The solvent is distilled off and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane → dichloromethane : methanol = 50 : 1), and recrystallized from ethanol to give 3-carboxy-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.4 g) as white powder, m.p. 221 - 223°C.

Example 386

To 3-carboxy-1-[4-(3,5-dichlorobenzoylamino)-benzoyl]-1,2,3,4-tetrahydroquinoline (3.7 g) are added tetrahydrofuran (50 ml) and thionyl chloride (5 ml). The mixture is reacted at 60°C for 1 hour. The reaction mixture is concentrated and to the residue is added acetone (20 ml). To the mixture is added dropwise a solution of sodium azide (1.0 g) in water (5 ml) under ice-cooling. The reaction mixture is stirred at the same temperature for 30 minutes and extracted with dichloromethane, dried over magnesium sulfate. The solvent is concentrated and to the resulting residue are added anhydrous toluene (30 ml) and benzyl alcohol (1.7 g). The mixture is refluxed for 1 hour. The reaction mixture is concentrated and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane → dichloromethane : methanol = 50 : 1) to give 3-benzyloxycarbonylamino-1-[4-(3,5-dichlorobenzoylamino)benzoyl)-1,2,3,4-tetrahydroquinoline (3.7 g) as colorless amorphous.

^{1}H-NMR ($CDCl_3$) δ : 2.80 (1H, dd, J=16.1 Hz, 5.3 Hz), 3.16 (1H, dd, J=15.8 Hz, 5.3 Hz), 3.75-4.50 (3H, m), 4.87-5.10 (3H, m), 6.80-7.60 (14H, m), 7.74 (2H, d, J=1.9 Hz), 8.47 (1H, brs)

Example 387

To 3-benzyloxycarbonylamino-1-[4-(3,5-dichloro-benzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (3.3 g)

are added acetic acid (40 ml) and 10 % Pd-C (0.4 g) and the reaction mixture is subjected to catalytic reduction at ordinary temperature under atmospheric pressure of hydrogen. One hour thereafter, the catalyst is removed by filtration and the filtrate is concentrated. The resulting residue is purified by silica gel column chromatography (eluent; dichloromethane : methanol = 20 : 1), and recrystallized from ethanol to give 3-amino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (1.6 g) as white powder, m.p. 207 - 210°C.

Example 388

To 3-amino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.5 g) are added methanol (10 ml), 37 % formaline (0.8 ml) and sodium cyanoborohydride (0.16 g). To the mixture is added acetic acid (0.5 ml) under ice-cooling and the mixture is stirred at room temperature for 1 hour. Water is added to the reaction mixture and the mixture is basified with potassium carbonate and extracted with dichloromethane. The solvent is concentrated and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane → dichloromethane : methanol = 20 : 1) to give 3-dimethylamino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.3 g) as colorless amorphous.

^{1}H-NMR ($CDCl_3$) δ : 2.35 (6H, s), 2.72-3.10 (3H, m), 3.65-3.78 (1H, m), 4.06-4.18 (1H, m), 6.60-7.62 (9H, m),

7.74 (2H, d, J=1.8 Hz), 8.52 (1H, brs)

Using the suitable starting materials, the compounds of the above Examples 246, 247, 375 and 376 are obtained in the same manner as in Example 388.

Example 389

To 3-amino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.44 g) are added dichloromethane (5 ml) and acetic anhydride (0.12 g) and the mixture is stirred for 1 hour. The reaction mixture is concentrated and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane → dichloromethane : methanol = 50 : 1) to give 3-acetylamino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.3 g) as colorless amorphous.

^{1}H-NMR ($CDCl_3$) δ : 1.87 (3H, s), 2.68 (1H, dd, J=5.6 Hz, 16 Hz), 3.14 (1H, dd, J=5.6 Hz, 16 Hz), 3.70-3.95 (2H, m), 4.32-4.50 (1H, m), 6.29 (1H, d, J=7.6 Hz), 6.90-7.80 (11H, m), 9.16 (1H, brs)

Using the suitable starting materials, the compound of the above Example 242 is obtained in the same manner as in Example 389.

Example 390

To 4-oxo-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.5 g) are added 40 % solution of methylamine in methanol (5 ml), molecular sieves 4A (1 g) and dimethylformamide (6 ml), and the mixture is refluxed

for 4 hours. After cooling, the reaction mixture is filtered and to the filtrate is added sodium borohydride (80 mg), and the mixture is stirred at room temperature for 1 hour. The reaction mixture is concentrated and water is added to the resulting residue, and extracted with ethyl acetate. The solvent is concentrated and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane : methanol = 20 : 1) to give 4-methylamino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.2 g) as colorless amorphous.

^{1}H-NMR ($CDCl_3$) δ : 1.62 (1H, brs), 1.90-2.25 (2H, m), 2.55 (3H, s), 3.78 (1H, t, J=5.1 Hz), 3.95 (2H, t, J=6.7 Hz), 6.99 (1H, d, J=7.9 Hz), 6.90-7.13 (2H, m)

Using the suitable starting materials, the compounds of the above Examples 238, 239, 244, 247, 375 and 376 are obtained in the same manner as in Example 390.

Example 391

To 3-carboxy-1-[4-(3,5-dichlorobenzoylamino)-benzoyl]-1,2,3,4-tetrahydroquinoline (0.7 g) are added dimethylformamide (7 ml), diethyl cyanophosphate (0.3 ml) and dimethylamine hydrochloride (0.15 g). Further thereto is added triethylamine (0.8 ml) and the mixture is stirred at room temperature for 1 hour. Water is added to the reaction mixture and extracted with ethyl acetate. The solvent is concentrated and to the resulting residue is added diethyl ether. The precipitated crystal is collected by filtration

to give 3-dimethylamido-1-[4-(3,5-dichlorobenzoylamino)-benzoyl]-1,2,3,4-tetrahydroquinoline (0.5 g) as light yellow powder, m.p. 186 - 187°C.

Example 392

To a solution of 1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine (3.0 g) in dichloromethane (50 ml) is added succinic anhydride (1.4 g) and the mixture is stirred at room temperature for 4.5 hours. The reaction mixture is evaporated under reduced pressure in order to remove the solvent therefrom, and the resulting crystal is recrystallized from ethyl acetate to give 1-[4-(3-carboxy-propionylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (3.61 g) as colorless needles, m.p. 192°C.

Using the suitable starting materials, the compound of the above Example 253 is obtained in the same manner as in Example 392.

Example 393

1-[4-(3-Carboxypropionylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.5 g) is dissolved in dimethyl-formamide (1 ml) and thereto is added dropwise diethyl cyanophosphate (0.25 g) under ice-cooling. The mixture is stirred at room temperature for 30 minutes and then cooled again with ice. Thereto are added dropwise a solution of diethylamine (0.11 g) in dimethylformamide (1 ml) and triethylamine (0.34 g). The mixture is stirred at room temperature for 16 hours. The solvent is distilled off

under reduced pressure and water is added to the resulting residue. The mixture is extracted with dichloromethane. The organic layer is washed successively with diluted hydrochloric acid, water, saturated sodium hydrogen carbonate solution, water and saturated saline solution, and dried over magnesium sulfate. The solvent is distilled off under reduced pressure and the resulting residue is purified by silica gel column chromatography (eluent; ethyl acetate), and recrystallized from n-hexane/ethyl acetate to give 1-[4-(3-diethylaminocarbonylpropionylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.42 g) as colorless scales, m.p. 165 - 167°C.

Using the suitable starting materials, the compounds of the above Examples 255 - 263 are obtained in the same manner as in Example 393.

Example 394

To a solution of 1-[4-(2-chloroacetylamino)-benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (2.06 g) in dimethylformamide (5 ml) are added sodium iodide (0.90 g), potassium carbonate (1.1 g) and cyclohexylamine (0.89 g), and the mixture is stirred at room temperature for 2 hours. Dimethylformamide is distilled off under reduced pressure and water is added to the resulting residue. The mixture is extracted with dichloromethane. The organic layer is washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is

distilled off under reduced pressure and the resulting residue is purified by silica gel column chromatography (eluent; ethyl acetate), and recrystallized from n-hexane/-ethyl acetate to give 1-[4-(2-cyclohexylaminoacetylamino)-benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (2.03 g) as white powder, m.p. 139 - 142°C.

Using the suitable starting materials, the compounds of the above Examples 271 - 309 and 317 are obtained in the same manner as in Example 394.

Example 395

o-Cresol (0.36 g) is dissolved in dimethylsulfoxide (4 ml) containing sodium hydroxide powder (0.18 g) and thereto is added 1-[4-(2-chloroacetylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (1.03 g). The mixture is stirred at 90°C for 7.5 hours. The reaction mixture is poured into ice-water (300 ml) and the precipitated crystal is collected by filtration, washed with water, and purified by silica gel column chromatography (eluent; n-hexane : ethyl acetate = 2 : 1), and recrystallized from ethyl acetate to give 1-{4-[2-(2-methylphenoxy)acetylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (546 mg) as colorless scales, m.p. 172.5 - 175°C.

Using the suitable starting materials, the compounds of the above Examples 310 and 312 - 316 are obtained in the same manner as in Example 395.

Example 396

A mixture of 1-{4-[2-(6-bromohexyloxy)benzoyl-

amino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (2.00 g), sodium acetate (0.36 g), sodium iodide (0.55 g) and acetic acid (20 ml) is refluxed for 1 day. The solvent is distilled off and the resulting residue is extracted with ethyl acetate. The organic layer is washed successively with 2N aqueous sodium hydroxide solution and saturated saline solution, and dried over magnesium sulfate. The solvent is concentrated and the resulting residue is purified by silica gel column chromatography (eluent; chloroform : methanol = 500 : 1), and recrystallized from ethanol to give 1-{4-[2-(6-acetyloxyhexyloxy)benzoylamino]-benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (1.07 g) as white powder, m.p. 145 - 146°C.

Using the suitable starting materials, the compound of the above Example 360 is obtained in the same manner as in Example 396.

Example 397

A mixture of 1-{4-[2-(6-bromohexyloxy)benzoyl-amino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (0.70 g), diethylamine (0.16 ml), triethylamine (0.21 ml) and acetonitrile (20 ml) is refluxed overnight. The solvent is distilled off and the resulting residue is dissolved in chloroform, washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is distilled off and the resulting residue is purified by silica gel column chromatography (eluent;

chloroform : methanol = 200 : 1 → 50 : 1) and converted into the hydrochloride thereof in methanol. The product is recrystallized from methanol/diethyl ether to give 1-{4-[2-(6-diethylaminohexyloxy)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine hydrochloride (0.42 g) as white powder, m.p. 91 - 95°C.

Using the suitable starting materials, the compounds of the above Examples 330, 332, 333, 335, 336, 339, 341, 342, 344 - 349, 352 - 355, 357 and 366 are obtained in the same manner as in Example 397.

Example 398

A mixture of 1-{4-[2-(6-bromohexyloxy)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (4.00 g), potassium phthalimide (2.02 g) and dimethylformamide (100 ml) is stirred at 100°C for 5 hours. The reaction mixture is filtered and the filtrate is distilled off. The resulting residue is extracted with ethyl acetate and the organic layer is washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is distilled off and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane), and recrystallized from methanol/diethyl ether to give 1-{4-[2-(6-phthalimidohexyloxy)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (4.06 g) as white powder, m.p. 145 - 146.5°C.

Using the suitable starting materials, the

compounds of the above Examples 331, 340, 364 and 365 are obtained in the same manner as in Example 398.

Example 399

A mixture of 1-{4-[2-[6-phthalimidohexyloxy)-benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (3.75 g), hydrazine hydrate (0.44 ml) and ethanol (30 ml) is refluxed for 3.5 hours. The precipitated crystal is collected by filtration, dried and purified by silica gel column chromatography (eluent; chloroform : methanol : aqueous ammonia = 100 : 10 : 1), and recrystallized from methanol/diethyl ether to give 1-{4-[2-(6-aminohexyloxy)-benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (2.52 g) as white powder, m.p. 135.5 - 137.5°C.

Using the suitable starting materials, the compounds of the above Examples 284, 344 and 345 are obtained in the same manner as in Example 399.

Example 400

A mixture of 1-{4-[2-(6-aminohexyloxy)benzoyl-amino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (0.70 g), acetic anhydride (20 ml) and two drops of conc. sulfuric acid is stirred at room temperature for 3 hours. To the reaction mixture is added aqueous 2N aqueous sodium hydroxide solution under ice-cooling and the mixture is extracted with chloroform. The organic layer is washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is distilled off

and the resulting residue is purified by silica gel column chromatography (eluent; chloroform : methanol = 200 : 1), and recrystallized from methanol/diethyl ether to give 1-{4-[2-(6-acetylaminohexyloxy)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (0.60 g) as colorless needles, m.p. 171 - 172°C.

Example 401

A mixture of 1-{4-[2-(6-aminohexyloxy)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (0.70 g), benzoyl chloride (0.20 ml), triethylamine and dichloromethane (20 ml) is stirred at room temperature for 1 hour. The reaction mixture is washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is concentrated and the resulting residue is recrystallized from ethanol to give 1-{4-[2-(6-benzoylaminohexyloxy)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (0.71 g) as white powder, m.p. 178 - 178.5°C.

Using the suitable starting materials, the compounds of the above Examples 348 and 357 are obtained in the same manner as in Examples 400 and 401.

Example 402

A mixture of 1-[4-(2-ethoxycarbonylmethoxybenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (1.00 g), aqueous ammonia (100 ml), ammonium chloride (0.3 g) and methanol (150 ml) is heated at 100°C for 4 hours in a sealed

tube. The solvent is distilled off and the resulting residue is extracted with chloroform, washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is concentrated and the resulting residue is purified by silica gel column chromatography (eluent; chloroform : methanol = 50 : 1), and recrystallized from methanol/diethyl ether to give 1-[4-(2-carbamoylmethoxybenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.43 g) as white powder, m.p. 198 - 199°C.

Example 403

A mixture of 1-[4-(2-chloro-4-aminobenzoylamino)-benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.55 g), acetic anhydride (15 ml), acetic acid (5 ml) and a drop of sulfuric acid is stirred at room temperature for 1 hour. To the reaction mixture is added aqueous 2N aqueous sodium hydroxide solution and the mixture is extracted with chloroform. The extract is washed with saturated saline solution and dried over magnesium sulfate. The solvent is concentrated and the resulting residue is recrystallized from methanol/diethyl ether to give 1-[4-(2-chloro-4-acetylaminobenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.28 g) as white powder, m.p. 214 - 243°C.

Using the suitable starting materials, the compound of the above Example 44 is obtained in the same manner as in Example 403.

Example 404

A mixture of 1-[4-(1-benzyloxycarbonyl-4-piperidinylcarbonylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (8.00 g), 10 % Pd-C (0.8 g) and ethanol (250 ml) is subjected to catalytic hydrogenation at 50°C under 4 atm. of hydrogen pressure for 6 hours. The catalyst is removed by filtration and the filtrate is evaporated under reduced pressure. The resulting residue is extracted with ethyl acetate and washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is distilled off and the resulting residue is purified by silica gel column chromatography (eluent; chloroform : methanol : ammonium hydroxide = 50 : 10 : 1) to give 1-{4-[4-(4-piperidinyl)benzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (4.80 g), and a part (0.5 g) thereof is converted into the hydrochloride thereof in methanol. The hydrochloride is recrystallized from methanol/diethyl ether to give 1-{4-[4-(4-piperidinyl)-benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine hydrochloride (0.42 g) as white powder, m.p. 177 - 181.5°C.

Example 405

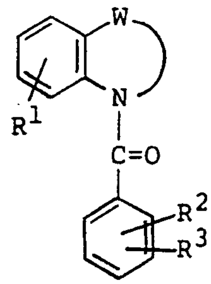
Using the suitable starting materials, the following compound is obtained in the same manner as in the above Examples 1, 382 and 388.

1-[4-(4-Dimethylaminobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline, colorless amorphous

^{1}H-NMR (DMSO-d_6) δ : 1.90-2.00 (2H, m), 2.82 (2H, t, J=6.5 Hz), 2.98 (6H, s), 3.77 (2H, t, J=6.5 Hz), 6.70-7.30 (6H, m), 7.32 (2H, d, J=8.6 Hz), 7.73 (2H, d, J=8.6 Hz), 8.00-8.20 (1H, m), 8.39 (1H, d, J=2.2 Hz), 10.37 (1H, s)

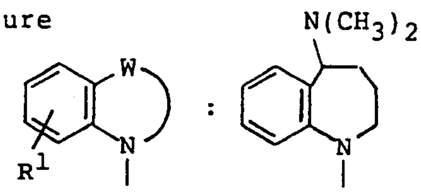
Using the suitable starting materials, the following compounds are obtained in the same manner as in Example 1.

Table 2

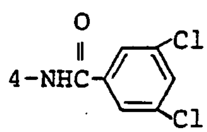


Example 406

Structure



R^2: H

R^3: 

Crystalline form: White powder

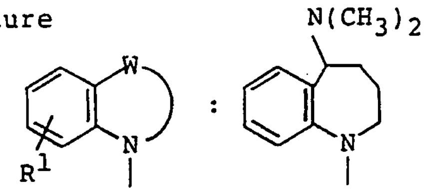
Recrystallization solvent: Ethanol

Melting Point: 216 - 218°C

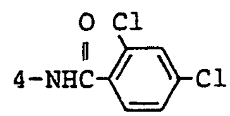
Form: Free

Example 407

Structure



R^2: H

R^3: 

Crystalline form: White powder

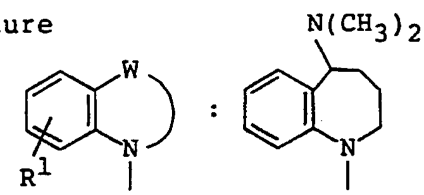
Recrystallization solvent: Ethanol

Melting Point: 181 - 183°C

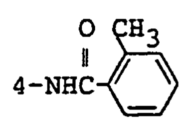
Form: Free

Example 408

Structure



R^2: H

R^3: 

Crystalline form: White powder

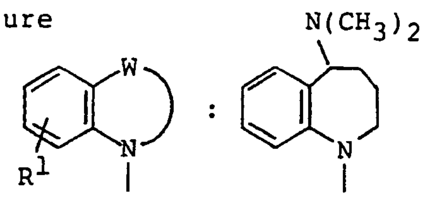
Recrystallization solvent: Ethanol

Melting Point: 207 - 208°C

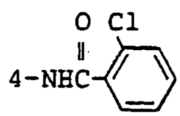
Form: Free

Example 409

Structure



R^2: H

R^3: 

Crystalline form: White powder

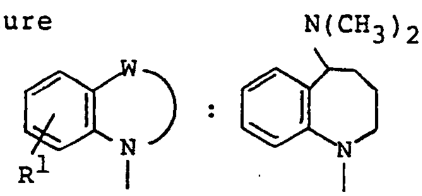
Recrystallization solvent: Ethanol

Melting Point: 213 - 214°C

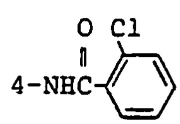
Form: Free

Example 410

Structure



R^2: 3-OCH_3

R^3: 

Crystalline form: White powder

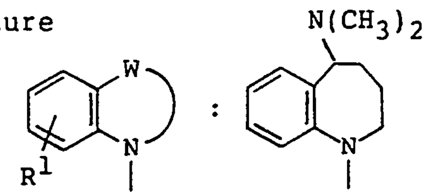
Recrystallization solvent: Ethanol

Melting Point: 136 - 138°C

Form: Free

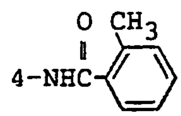
Example 411

Structure



R^2: 3-OCH_3

R^3:



Crystalline form: White powder

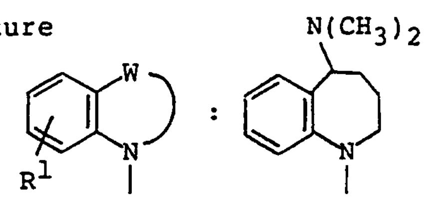
Recrystallization solvent: Ethanol

Melting Point: 130 - 132°C

Form: Free

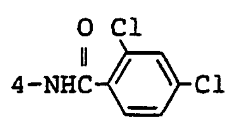
Example 412

Structure



R^2: 3-OCH_3

R^3:



Crystalline form: White powder

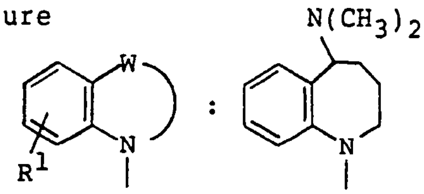
Recrystallization solvent: Ethanol

Melting Point: 143 - 145°C

Form: Free

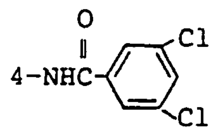
Example 413

Structure



R^2: 3-OCH_3

R^3:



Crystalline form: White powder

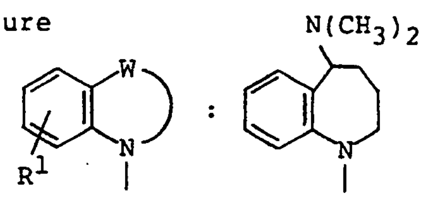
Recrystallization solvent: Ethanol

Melting Point: 171 - 173°C

Form: Free

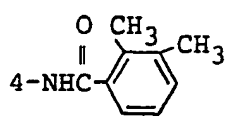
Example 414

Structure



R^2: 3-OCH_3

R^3:



Crystalline form: White powder

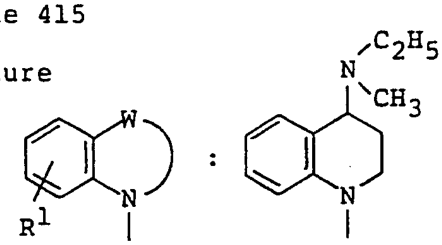
Recrystallization solvent: Ethanol

Melting Point: 162 - 164°C

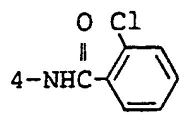
Form: Free

Example 415

Structure



R^2: H

R^3: 

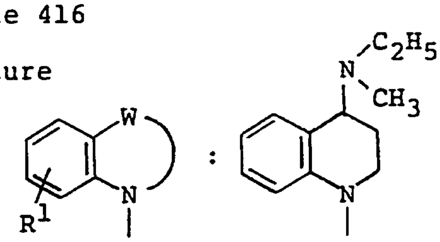
Crystalline form: Colorless amorphous

NMR analysis: 49)

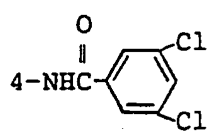
Form: Free

Example 416

Structure



R^2: H

R^3: 

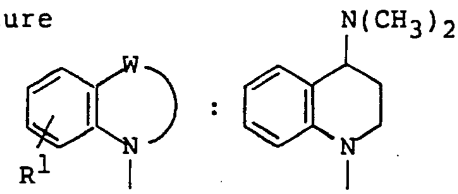
Crystalline form: Colorless amorphous

NMR analysis: 50)

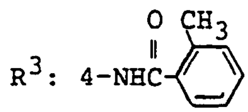
Form: Free

Example 417

Structure



R^2: 3-OCH_3



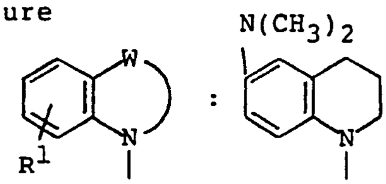
Crystalline form: Colorless amorphous

NMR analysis: 51)

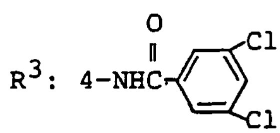
Form: Free

Example 418

Structure



R^2: H



Crystalline form: Colorless needles

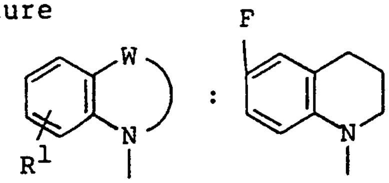
Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 228.5 - 230°C

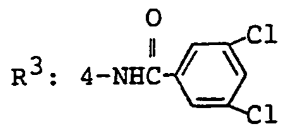
Form: Free

Example 419

Structure



R^2: H



Crystalline form: White powder

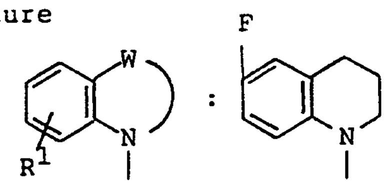
Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 205.5 - 206.5°C

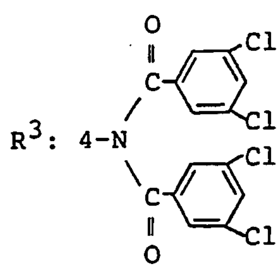
Form: Free

Example 420

Structure



R^2: H



Crystalline form: White powder

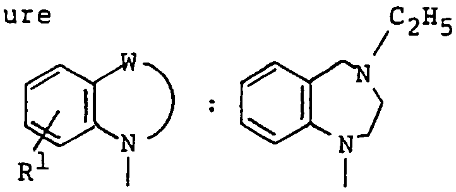
Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 210 - 212°C

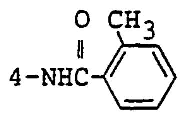
Form: Free

Example 421

Structure



R^2: H

R^3: 

Crystalline form: White powder

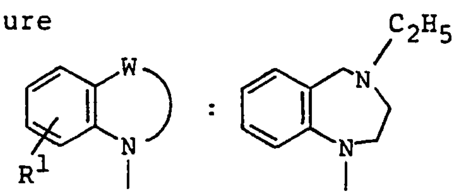
Recrystallization solvent: Ethanol

Melting Point: 166 - 167°C

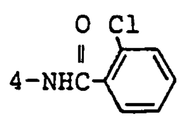
Form: Free

Example 422

Structure



R^2: H

R^3: 

Crystalline form: White powder

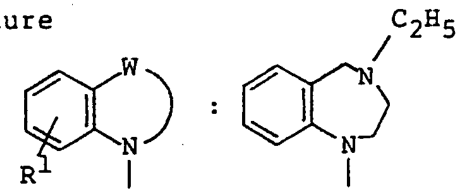
Recrystallization solvent: Ethanol

Melting Point: 191.5 - 192.5°C

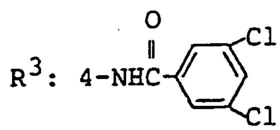
Form: Free

Example 423

Structure



R^2: H



Crystalline form: White powder

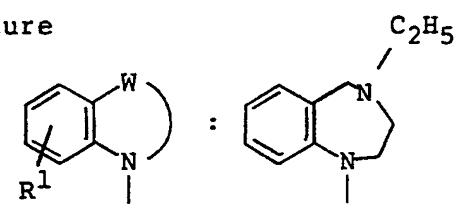
Recrystallization solvent: Ethanol

Melting Point: 209 - 210°C

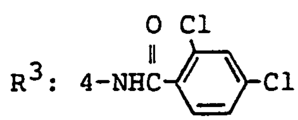
Form: Free

Example 424

Structure



R^2: H



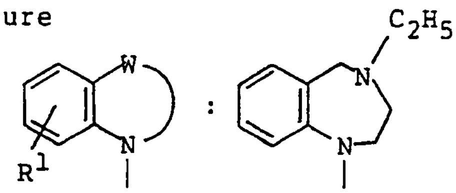
Crystalline form: Colorless amorphous

NMR analysis: 52)

Form: Free

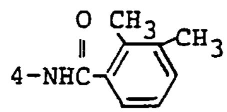
Example 425

Structure



R^2: H

R^3:



Crystalline form: White powder

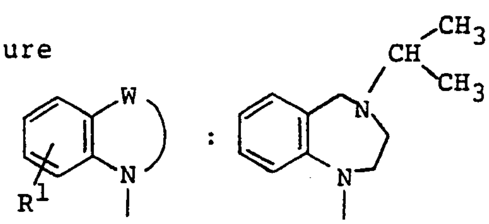
Recrystallization solvent: Ethanol

Melting Point: 148 - 149°C

Form: Free

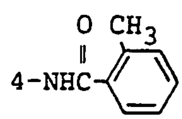
Example 426

Structure



R^2: H

R^3:



Crystalline form: White powder

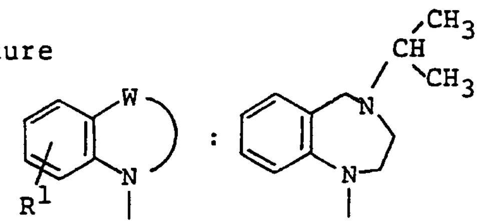
Recrystallization solvent: Ethanol

Melting Point: 157 - 158°C

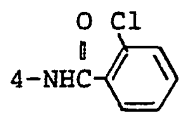
Form: Free

Example 427

Structure



R^2: H

R^3: 

Crystalline form: White powder

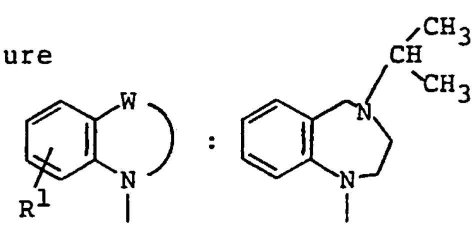
Recrystallization solvent: Ethanol

Melting Point: 194.5 - 195.5°C

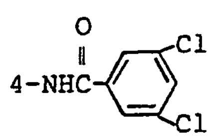
Form: Free

Example 1428

Structure



R^2: H

R^3: 

Crystalline form: White powder

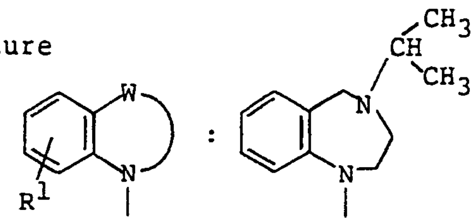
Recrystallization solvent: Ethanol

Melting Point: 179.5 - 180.5°C

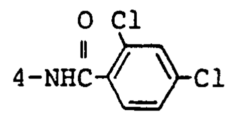
Form: Free

Example 429

Structure



R^2: H

R^3: 

Crystalline form: White powder

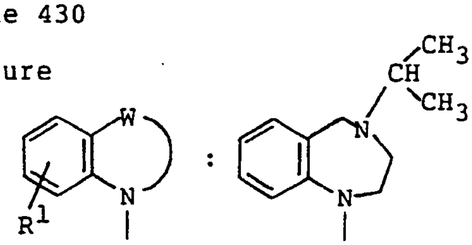
Recrystallization solvent: Ethanol

Melting Point: 190 - 191°C

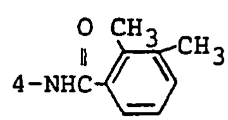
Form: Free

Example 430

Structure



R^2: H

R^3: 

Crystalline form: White powder

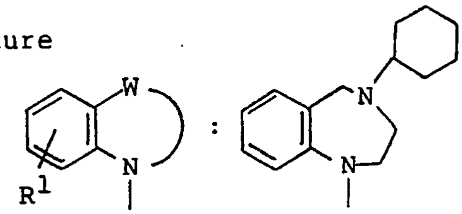
Recrystallization solvent: Ethanol

Melting Point: 159 - 160°C

Form: Free

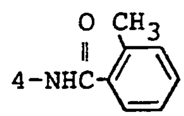
Example 431

Structure



R^2: H

R^3:



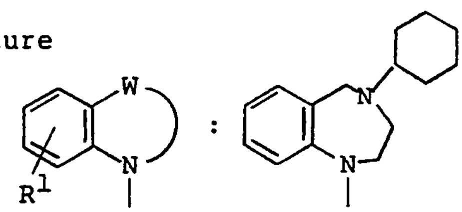
Crystalline form: Colorless amorphous

NMR analysis: 53)

Form: Hydrochloride

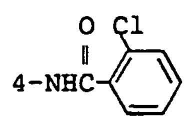
Example 432

Structure



R^2: H

R^3:



Crystalline form: White powder

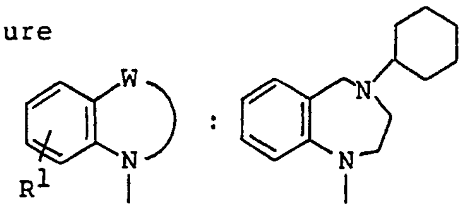
Recrystallization solvent: Ethanol

Melting Point: 155 - 156°C

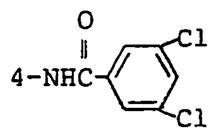
Form: Free

Example 433

Structure



R^2: H

R^3: 

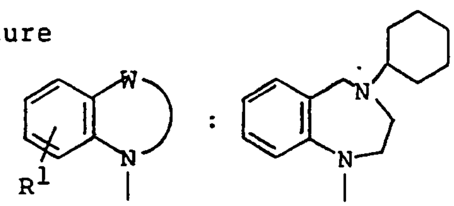
Crystalline form:Colorless amorphous

NMR analysis: 54)

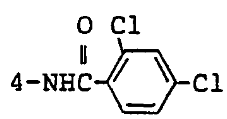
Form: Free

Example 434

Structure



R^2: H

R^3: 

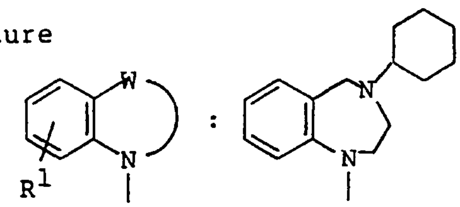
Crystalline form: Colorless amorphous

NMR analysis: 55)

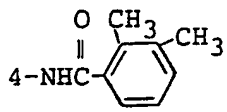
Form: Free

Example 435

Structure



R²: H

R³: 

Crystalline form: White powder

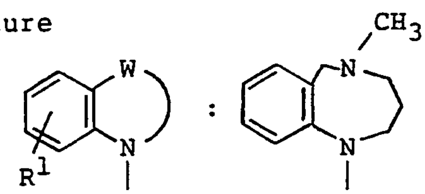
Recrystallization solvent: Ethanol

Melting Point: 175 - 177°C

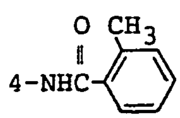
Form: Free

Example 436

Structure



R²: H

R³: 

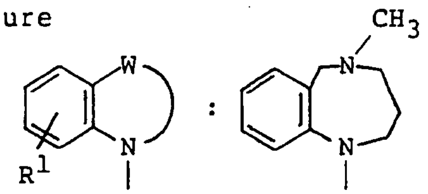
Crystalline form: Colorless amorphous .

NMR analysis: 56)

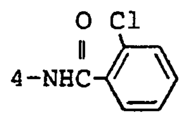
Form: Free

Example 437

Structure



R^2: H

R^3: 

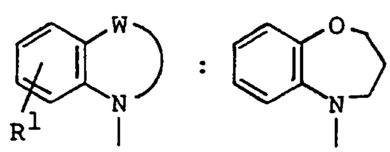
Crystalline form: Colorless amorphous

NMR analysis: 57)

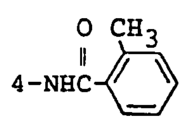
Form: Free

Example 438

Structure



R^2: H

R^3: 

Crystalline form: White powder

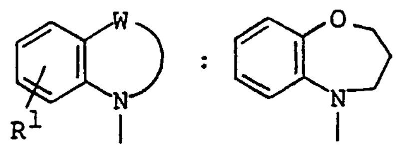
Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 219 - 220°C

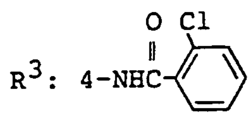
Form: Free

Example 439

Structure



R^2: H



Crystalline form: White powder

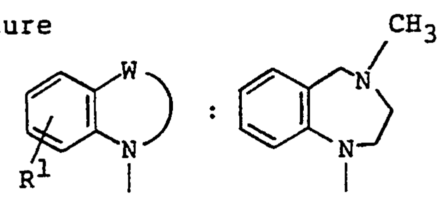
Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 215 - 218°C

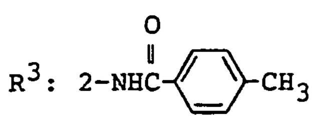
Form: Free

Example 440

Structure



R^2: H



Crystalline form: White powder

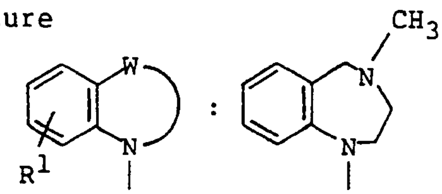
Recrystallization solvent: Ethanol

Melting Point: 128.5 - 129.5°C

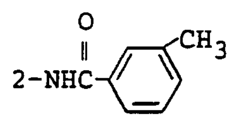
Form: Free

Example 441

Structure



R^2: H

R^3: 

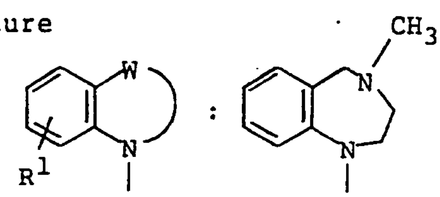
Crystalline form: Colorless amorphous

NMR analysis: 58)

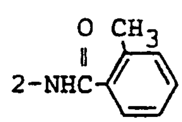
Form: Free

Example 442

Structure



R^2: H

R^3: 

Crystalline form: White powder

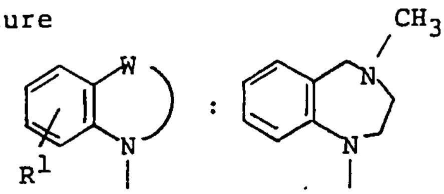
Recrystallization solvent: Ethanol

Melting Point: 153 - 154°C

Form: Free

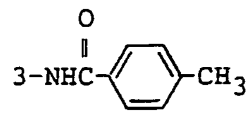
Example 443

Structure



R^2: H

R^3:



Crystalline form: White powder

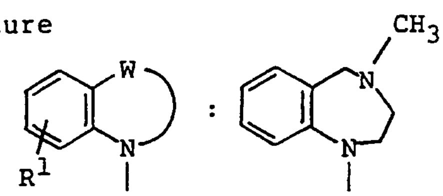
Recrystallization solvent: Ethanol

Melting Point: 150 - 153°C

Form: Free

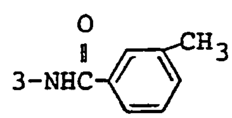
Example 444

Structure



R^2: H

R^3:



Crystalline form: White powder

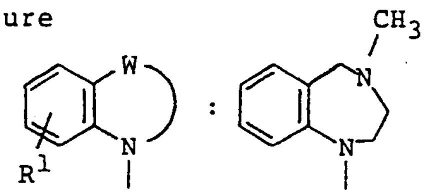
Recrystallization solvent: Ethanol

Melting Point: 139 - 141°C

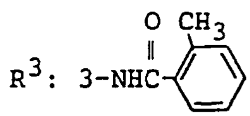
Form: Free

Example 445

Structure



R^2: H



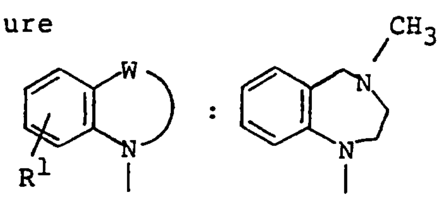
Crystalline form: Colorless amorphous

NMR analysis: 59)

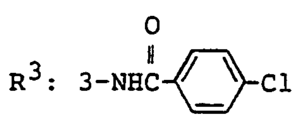
Form: Free

Example 446

Structure



R^2: H



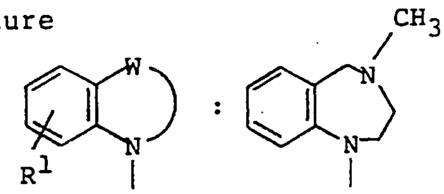
Crystalline form: Colorless amorphous

NMR analysis: 60)

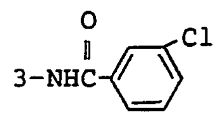
Form: Free

Example 447

Structure



R^2: H

R^3: 

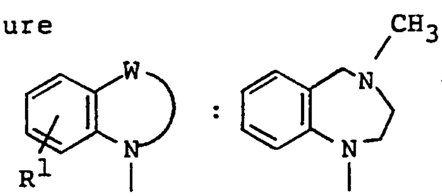
Crystalline form: Colorless amorphous

NMR analysis: 61)

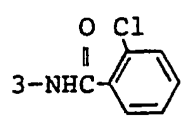
Form: Free

Example 448

Structure



R^2: H

R^3: 

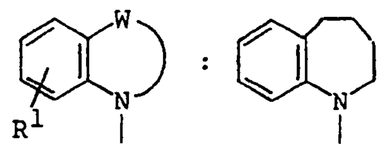
Crystalline form: Colorless amorphous

NMR analysis: 62)

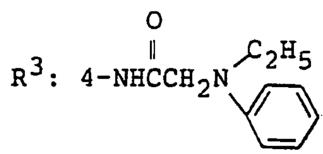
Form: Free

Example 449

Structure



R^2: 3-OCH_3



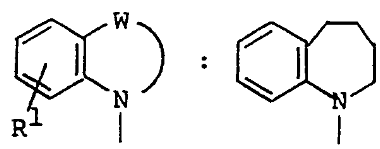
Crystalline form: Colorless amorphous

NMR analysis: 63)

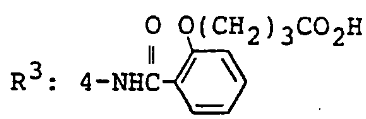
Form: Free

Example 450

Structure



R^2: H



Crystalline form: White powder

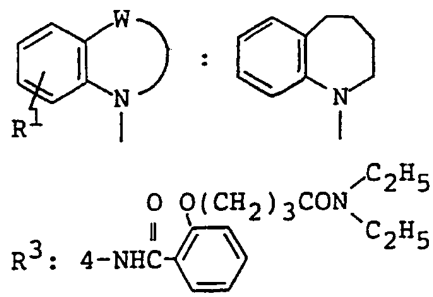
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 172.5 - 173.5°C

Form: Free

Example 451

Structure



R^2: H

Crystalline form: Colorless prisms

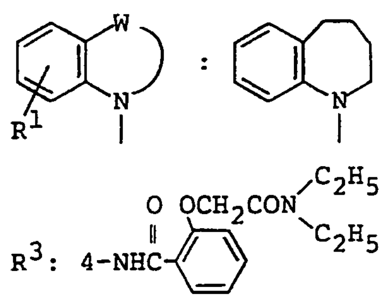
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 122.5 - 123°C

Form: Free

Example 452

Structure



R^2: H

Crystalline form: White powder

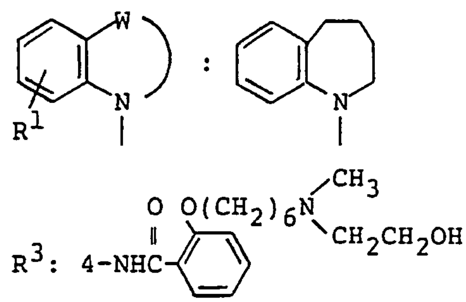
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 198 - 199.5°C

Form: Free

Example 453

Structure



R^2: H

Crystalline form: White powder

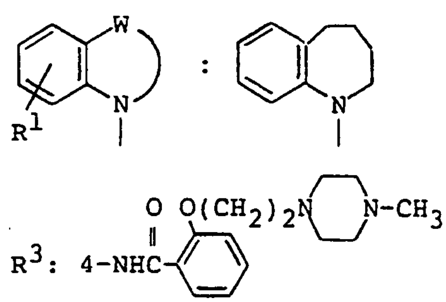
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 118 - 119.5°C

Form: Hydrochloride

Example 454

Structure



R^2: H

Crystalline form: White powder

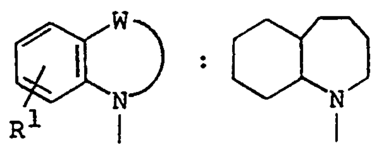
Recrystallization solvent: Ethanol

Melting Point: 163 - 165°C

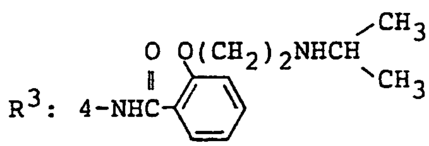
Form: Dihydrochloride

Example 455

Structure



R^2: H



Crystalline form: White powder

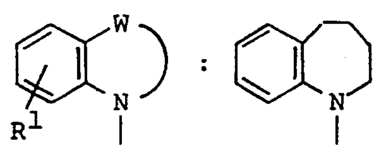
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 246 - 248°C

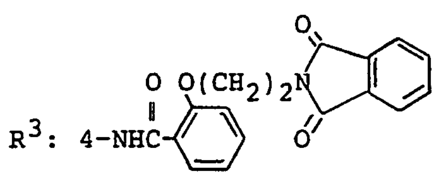
Form: Hydrochloride

Example 456

Structure



R^2: H



Crystalline form: White powder

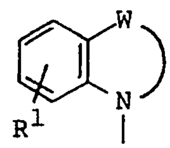
Recrystallization solvent: Chloroform/ethanol

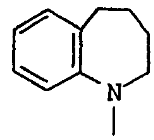
Melting Point: 204 - 205°C

Form: Free

Example 457

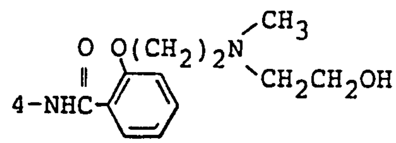
Structure





R^2: H

R^3:



Crystalline form: Colorless prisms

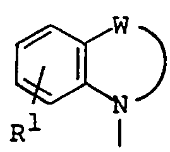
Recrystallization solvent: Methanol/diethyl ether

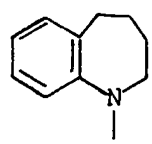
Melting Point: 127 - 128°C

Form: Hydrochloride

Example 458

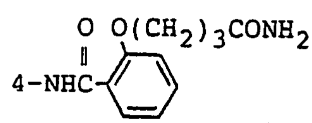
Structure





R^2: H

R^3:



Crystalline form: White powder

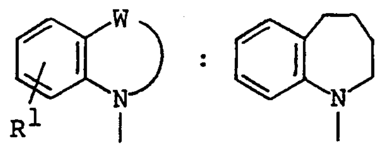
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 220 - 221°C

Form: Free

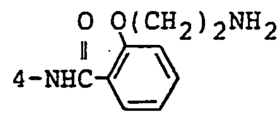
Example 459

Structure



R^2: H

R^3:



Crystalline form: Colorless needles

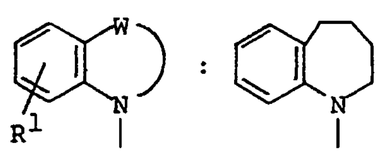
Recrystallization solvent: Ethanol

Melting Point: 190 - 192°C

Form: Free

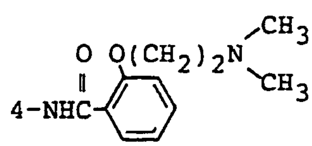
Example 460

Structure



R^2: H

R^3:



Crystalline form: White powder

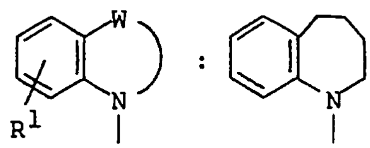
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 189 - 191°C

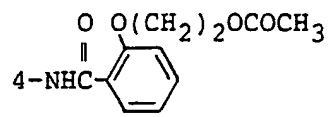
Form: Hydrochloride

Example 461

Structure



R^2: H

R^3: 

Crystalline form: Colorless needles

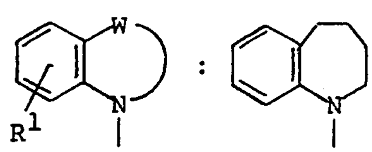
Recrystallization solvent: Ethanol

Melting Point: 173 - 174°C

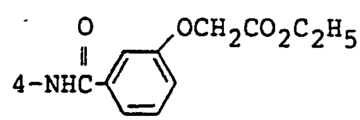
Form: Free

Example 462

Structure



R^2: H

R^3: 

Crystalline form: White powder

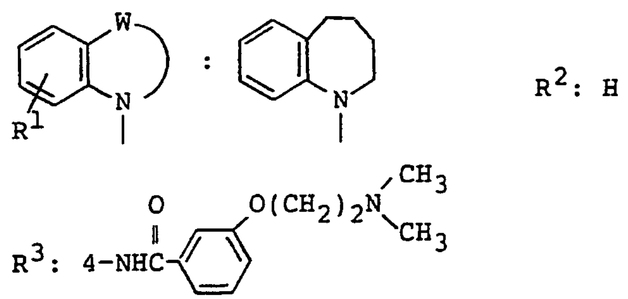
Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 129 - 130°C

Form: Free

Example 463

Structure



Crystalline form: White powder

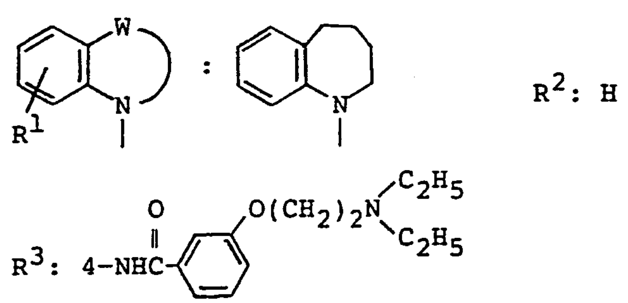
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 130 - 133°C

Form: Hydrochloride

Example 464

Structure



Crystalline form: Light yellow powder

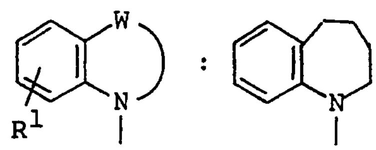
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 170.5 - 172°C

Form: Hydrochloride

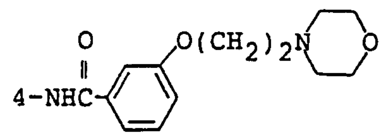
Example 465

Structure



R^2: H

R^3:



Crystalline form: White powder

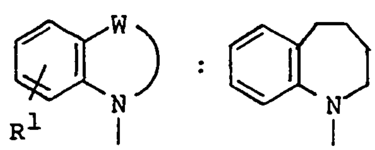
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 126 - 131°C

Form: Hydrochloride

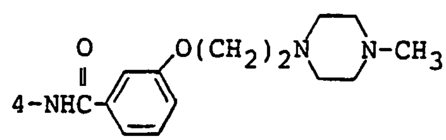
Example 466

Structure



R^2: H

R^3:



Crystalline form: White powder

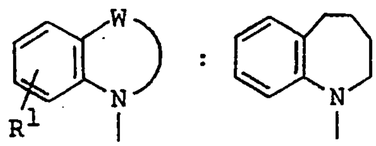
Recrystallization solvent: Ethanol

Melting Point: 182 - 185°C

Form: Dihydrochloride

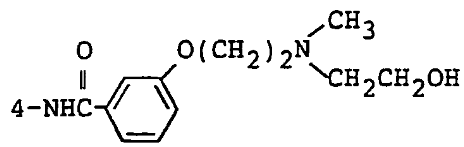
Example 467

Structure



R^2: H

R^3:



Crystalline form: White powder

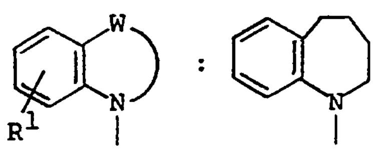
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 116 - 121°C

Form: Hydrochloride

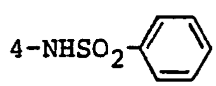
Example 468

Structure



R^2: H

R^3:



Crystalline form: Colorless prisms

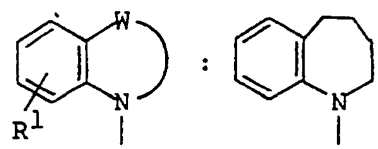
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 178 - 182.5°C

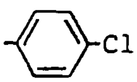
Form: Free

Example 469

Structure



R^2: H

R^3: 4-$NHSO_2$- 

Crystalline form: Colorless particles

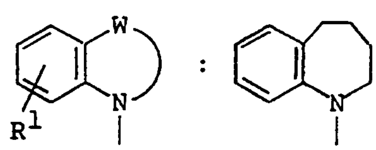
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 185 - 187°C

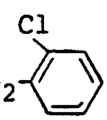
Form: Free

Example 470

Structure



R^2: H

R^3: 4-$NHSO_2$- 

Crystalline form: White powder

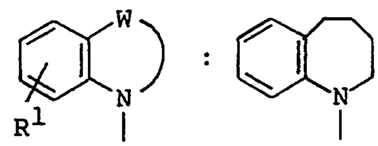
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 215 - 217°C

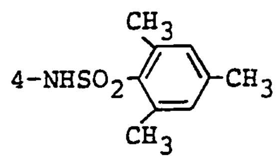
Form: Free

Example 471

Structure



R^2: H

R^3: 

Crystalline form: White powder

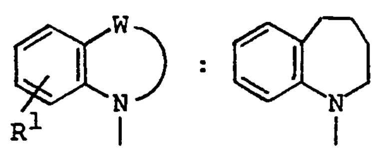
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 176 - 178°C

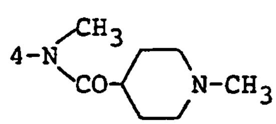
Form: Free

Example 472

Structure



R^2: H

R^3: 

Crystalline form: Light yellow powder

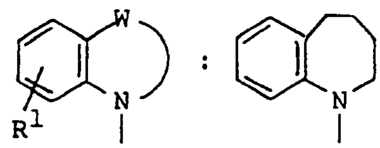
Recrystallization solvent: Methanol/n-hexane

Melting Point: 194.5 - 197°C

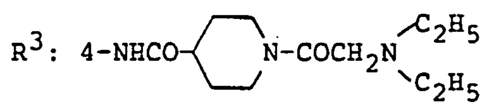
Form: Free

Example 473

Structure



R^2: H



Crystalline form: White powder

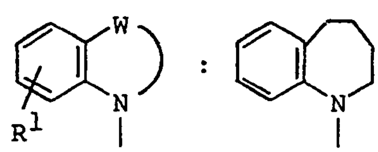
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 161.5 - 165.5°C

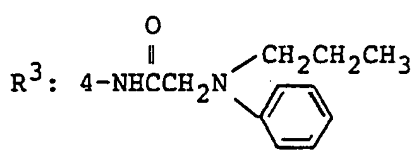
Form: Hydrochloride

Example 474

Structure



R^2: H



Crystalline form: White powder

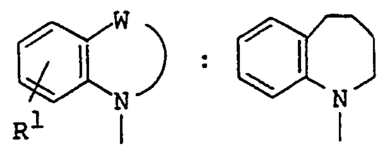
Recrystallization solvent: Ethyl acetate

Melting Point: 152 - 153°C

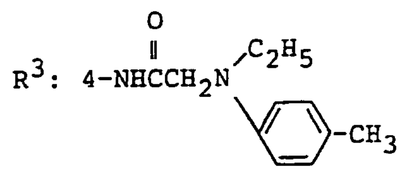
Form: Free

Example 475

Structure



R^2: H



Crystalline form: Colorless needles

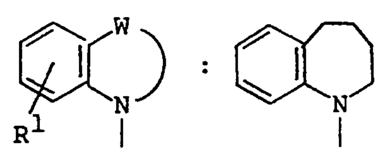
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 147 - 148°C

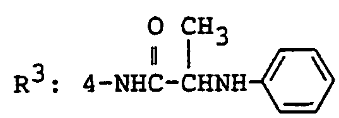
Form: Free

Example 476

Structure



R^2: H



Crystalline form: Light yellow powder

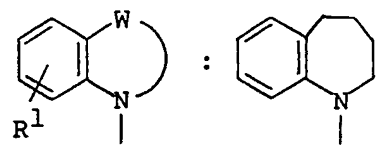
Recrystallization solvent: Ethyl acetate

Melting Point: 215 - 217°C

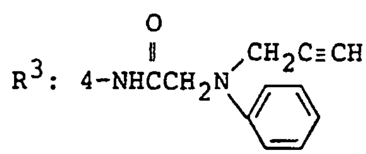
Form: Free

Example 477

Structure



R^2: H



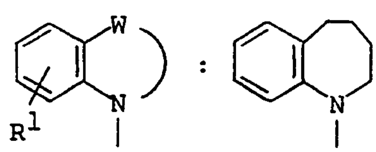
Crystalline form: Colorless amorphous

NMR analysis: 64)

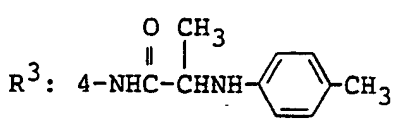
Form: Free

Example 478

Structure



R^2: H



Crystalline form: White powder

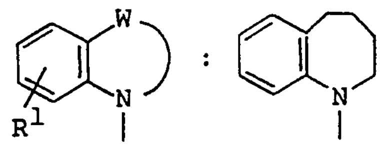
Recrystallization solvent: Ethyl acetate

Melting Point: 180 - 181°C

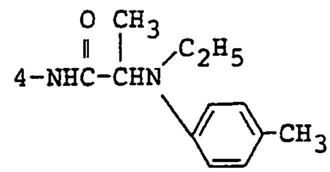
Form: Free

Example 479

Structure



R^2: H

R^3: 

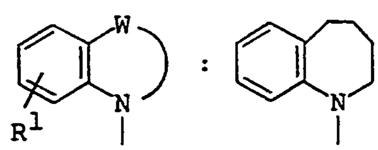
Crystalline form: Colorless amorphous

NMR analysis: 65)

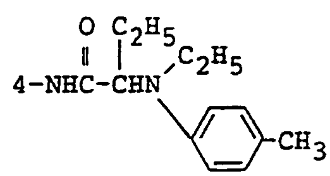
Form: Free

Example 480

Structure



R^2: H

R^3: 

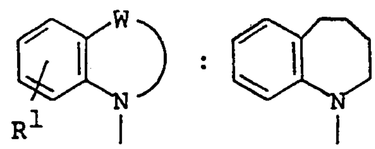
Crystalline form: Colorless amorphous

NMR analysis: 66)

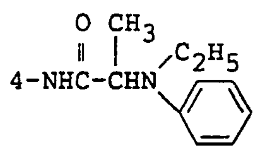
Form: Free

Example 481

Structure



R^2: H

R^3: 

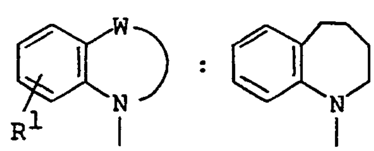
Crystalline form: Colorless amorphous

NMR analysis: 67)

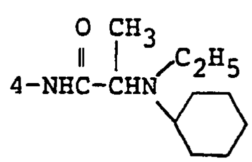
Form: Free

Example 482

Structure



R^2: H

R^3: 

Crystalline form: Colorless scales

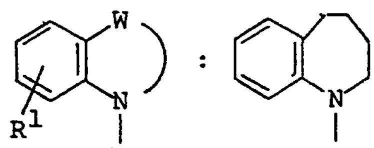
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 165 - 167°C

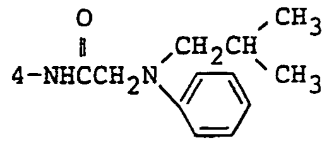
Form: Free

Example 483

Structure



R^2: H

R^3: 

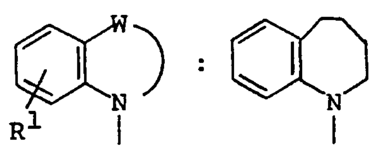
Crystalline form: Colorless amorphous

NMR analysis: 68)

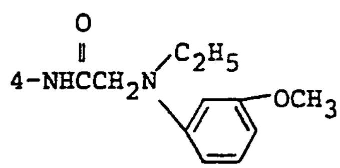
Form: Free

Example 484

Structure



R^2: H

R^3: 

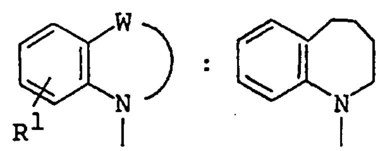
Crystalline form: Colorless amorphous

NMR analysis: 69)

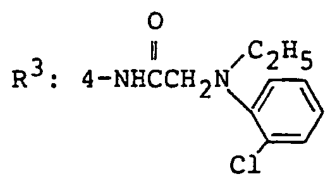
Form: Free

Example 485

Structure



R^2: H



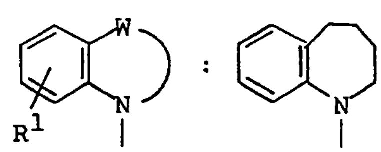
Crystalline form: Colorless amorphous

NMR analysis: 70)

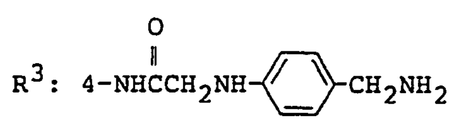
Form: Free

Example 486

Structure



R^2: H



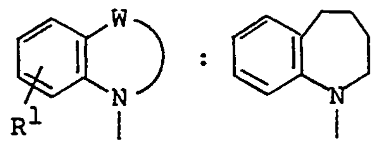
Crystalline form: Colorless amorphous

NMR analysis: 71)

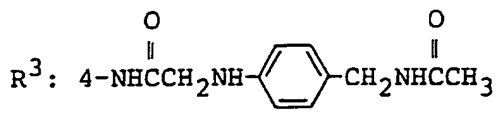
Form: Free

Example 487

Structure



R^2: H



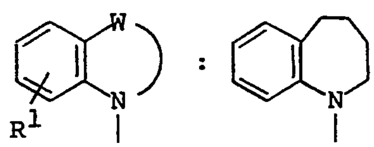
Crystalline form: Colorless amorphous

NMR analysis: 72)

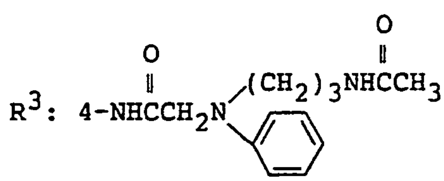
Form: Free

Example 488

Structure



R^2: H



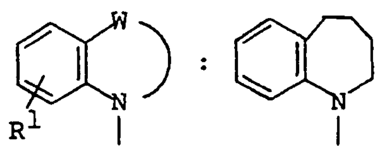
Crystalline form: Colorless amorphous

NMR analysis: 73)

Form: Free

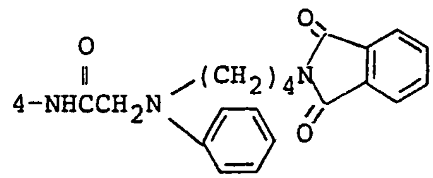
Example 489

Structure



R^2: H

R^3:



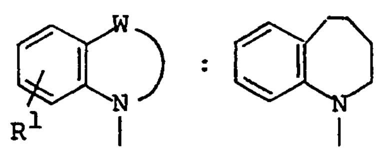
Crystalline form: Light yellow amorphous

NMR analysis: 74)

Form: Free

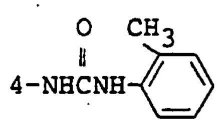
Example 490

Structure



R^2: H

R^3:



Crystalline form: White powder

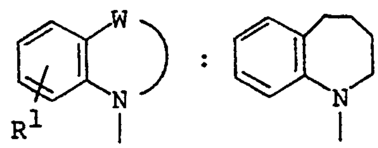
Recrystallization solvent: Ethyl acetate

Melting Point: 182 - 182.5°C

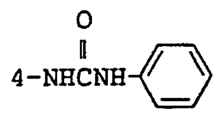
Form: Free

Example 491

Structure



R^2: H

R^3: 

Crystalline form: White powder

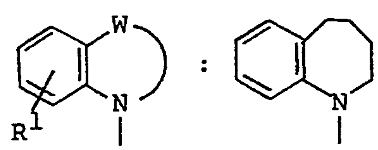
Recrystallization solvent: Ethyl acetate

Melting Point: 244 - 245°C

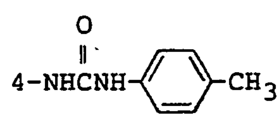
Form: Free

Example 492

Structure



R^2: H

R^3: 

Crystalline form: White powder

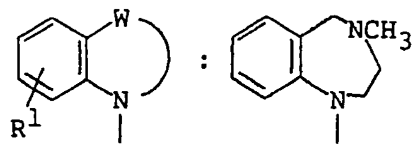
Recrystallization solvent: Ethyl acetate

Melting Point: 220 - 221.5°C

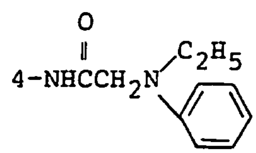
Form: Free

Example 493

Structure



R^2: H

R^3: 

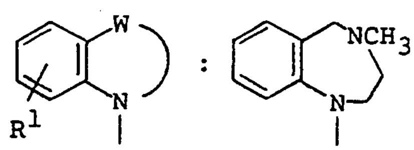
Crystalline form: Light yellow amorphous

NMR analysis: 75)

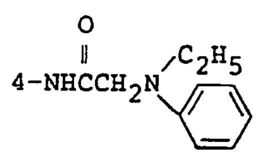
Form: Free

Example 494

Structure



R^2: 3-OCH_3

R^3: 

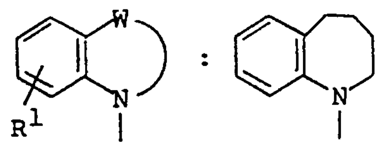
Crystalline form: Light yellow amorphous

NMR analysis: 76)

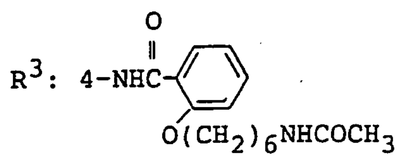
Form: Free

Example 495

Structure



R^2: H



Crystalline form: Colorless needles

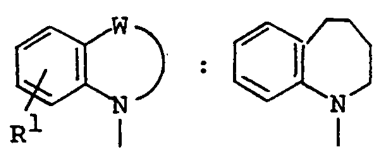
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 171 - 172°C

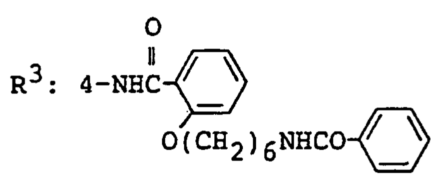
Form: Free

Example 496

Structure



R^2: H



Crystalline form: White powder

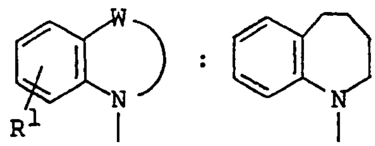
Recrystallization solvent: Ethanol

Melting Point: 178 - 178.5°C

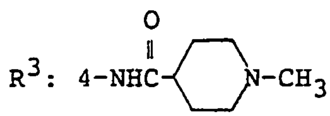
Form: Free

Example 497

Structure

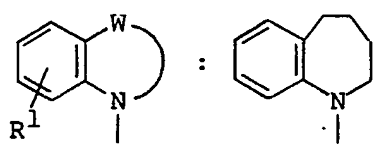


R^2: H

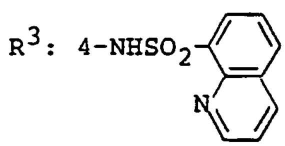


Example 498

Structure

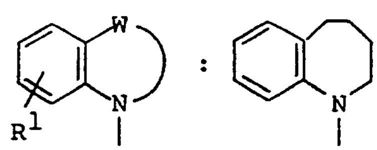


R^2: H

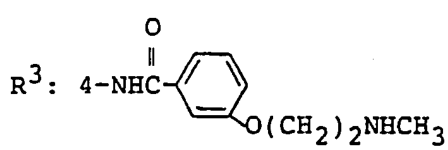


Example 499

Structure

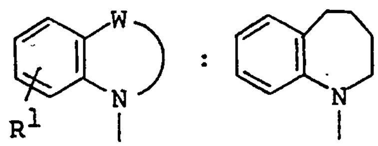


R^2: H

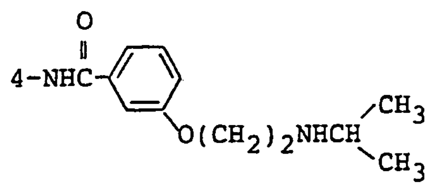


Example 500

Structure

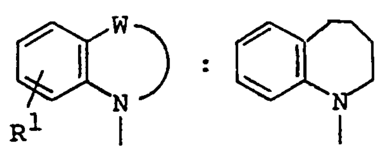


R^2: H

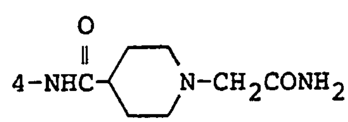
R^3: 

Example 501

Structure

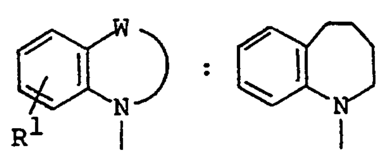


R^2: H

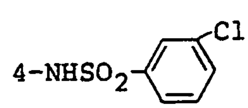
R^3: 

Example 502

Structure

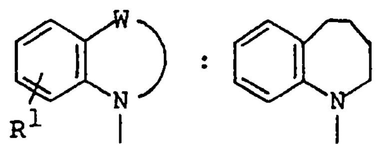


R^2: H

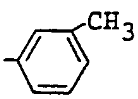
R^3: 

Example 503

Structure

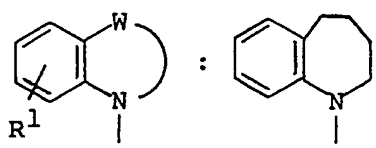


R^2: H

R^3: 4-$NHSO_2$-

Example 504

Structure



R^2: H

R^3: 4-$NHC(=O)CH_2COOH$

Crystalline form: Light yellow scales

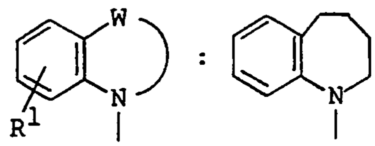
Recrystallization solvent: Ethanol/water

Melting Point: 129 - 131°C

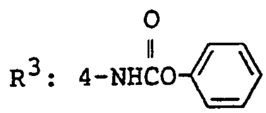
Form: Free

Example 505

Structure



R^2: H



Crystalline form: White powder

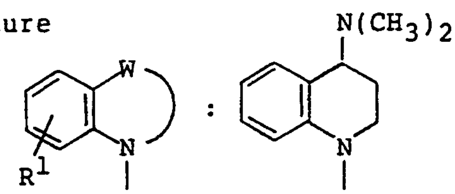
Recrystallization solvent: Ethyl acetate

Melting Point: 199 - 201°C

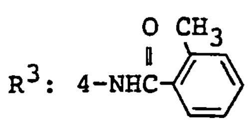
Form: Free

Example 506

Structure



R^2: H



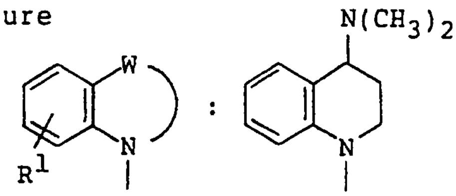
Crystalline form: Colorless amorphous

NMR analysis: 77)

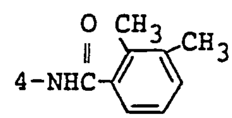
Form: Free

Example 507

Structure



R^2: H

R^3: 

Crystalline form: White powder

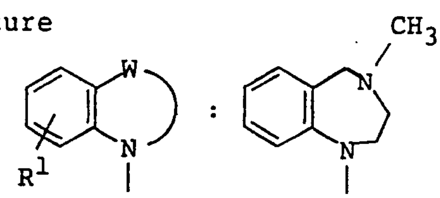
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 187.5 - 189°C

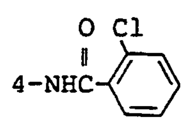
Form: Free

Example 508

Structure



R^2: 2-Cl

R^3: 

Crystalline form: White powder

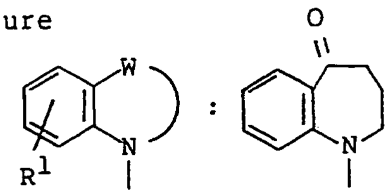
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 161 - 164°C

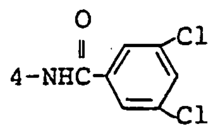
Form: Free

Example 509

Structure



R^2: H

R^3: 

Crystalline form: Colorless prisms

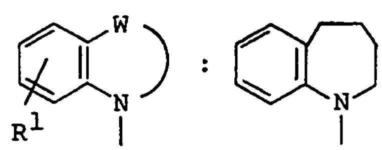
Recrystallization solvent: Ethanol

Melting Point: 242 - 243°C

Form: Free

Example 510

Structure



R^2: 3-OCH_3

R^3: 4-$NHCOCH_2Cl$

Crystalline form: White powder

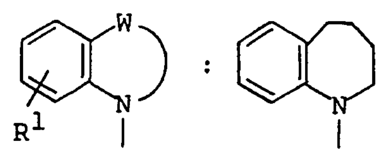
Recrystallization solvent: Dichloroethane/diethyl ether

Melting Point: 186 - 188°C

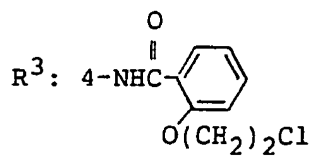
Form: Free

Example 511

Structure



R^2: H



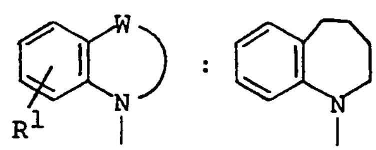
Crystalline form: Colorless amorphous

NMR analysis: 78)

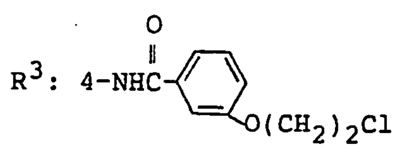
Form: Free

Example 512

Structure



R^2: H



Crystalline form: Colorless amorphous

NMR analysis: 79)

Form: Free

49) ^{1}H-NMR($CDCl_3$) δ ; 1.11 (3H, t, J=7.1 Hz), 1.90-2.25 (2H, m), 2.29 (3H, s), 2.55 (2H, q, J=7.1 Hz), 3.62-3.90 (2H, m), 4.00-4.20 (1H, m), 6.63 (1H, d, J=7.9 Hz), 6.85-7.10 (2H, m), 7.25-7.80 (9H, m), 8.25 (1H, brs)

50) ^{1}H-NMR($CDCl_3$) δ ; 1.10 (3H, t, J=7.1 Hz), 1.90-2.20 (2H, m), 2.28 (3H, s), 3.60-3.90 (2H, m), 3.95-4.20 (1H, m), 6.62 (1H, d, J=7.9 Hz), 6.80-7.10 (2H, m), 7.20 (2H, d, J=8.6 Hz), 7.31-7.55 (4H, m), 7.80 (2H, d, J=1.9 Hz), 9.05 (1H, brs)

51) ^{1}H-NMR($CDCl_3$) δ ; 1.80-2.05 (1H, m), 2.15-2.50 (1H, m), 2.34 (6H, s), 2.51 (3H, s), 3.48-3.62 (1H, m), 3.72 (3H, s), 3.70-3.85 (1H, m), 4.00-4.22 (1H, m), 6.64 (1H, d, J=7.8 Hz), 6.84-7.58 (9H, m), 8.16 (1H, brs), 8.40 (1H, d, J=8.7 Hz)

52) ^{1}H-NMR($CDCl_3$) δ ; 1.16 (3H, t, J=7.1 Hz), 2.40-2.70 (2H, m), 2.90-3.30 (3H, m), 3.80-4.20 (2H, m), 4.80-5.00 (1H, m), 6.60-6.80 (1H, m), 7.00-7.70 (10H, m), 8.24 (1H, s)

53) ^{1}H-NMR(DMSO-d_6) δ ; 1.0-2.5 (10H, m), 2.34 (3H, s), 3.30-3.80 (4H, m), 4.50-5.30 (3H, m), 6.70-7.00 (1H, m), 7.10-7.80 (11H, m), 10.43 (1H, s), 10.5-12.0 (1H, br)

54) ^{1}H-NMR($CDCl_3$) δ ; 1.10-2.10 (10H, m), 2.40-2.70 (1H, m), 2.80-3.20 (3H, m), 3.92 (2H, s), 4.90-5.20 (1H, m), 6.50-6.70 (1H, m), 6.80-7.60 (8H, m), 7.75

(2H, s), 8.73 (1H, s)

55) ^{1}H-NMR($CDCl_3$) δ ; 1.10-2.20 (10H, m), 2.40-2.70 (1H, m), 2.90-3.30 (3H, m), 3.93 (2H, s), 4.90-5.20 (1H, m), 6.62 (1H, d, J=7.6 Hz), 6.90-7.70 (10H, m), 8.29 (1H, s)

56) ^{1}H-NMR($CDCl_3$) δ ; 1.50-2.10 (2H, m), 2.38 (6H, s), 2.30-2.70 (1H, m), 2.70-3.00 (2H, m), 3.45 (1H, d, J=13 Hz), 3.81 (1H, d, J=14 Hz), 4.70-5.00 (1H, m), 7.0-7.50 (12H, m), 8.23 (1H, s)

57) ^{1}H-NMR($CDCl_3$) δ ; 1.50-2.10 (2H, m), 2.42 (3H, s), 2.40-2.70 (1H, m), 2.80-3.00 (2H, m), 3.52 (1H, d, J=13 Hz), 3.85 (1H, d, J=13 Hz), 4.70-5.00 (1H, m), 7.00-7.70 (12H, m), 8.54 (1H, s)

58) ^{1}H-NMR($CDCl_3$) δ ; 2.43 (3H, s), 2.47 (3H, s), 3.00-3.30 (3H, m), 3.76 (1H, d, J=14 Hz), 4.06 (1H, d, J=14 Hz), 4.90-5.20 (1H, m), 6.50-6.80 (3H, m), 6.90-7.50 (6H, m), 7.70-8.00 (2H, m), 8.48 (1H, d, J=8 Hz), 10.58 (1H, s)

59) ^{1}H-NMR($CDCl_3$) δ ; 2.41 (3H, s), 2.44 (3H, s), 2.90-3.20 (3H, m), 3.74 (1H, d, J=13 Hz), 4.07 (1H, d, J=14 Hz), 4.80-5.00 (1H, m), 6.67 (1H, d, J=7 Hz), 6.76 (1H, d, J=7 Hz), 7.00-7.50 (8H, m), 7.55 (1H, s), 7.70-7.90 (2H, m)

60) ^{1}H-NMR($CDCl_3$) δ ; 2.41 (3H, s), 2.80-3.20 (3H, m), 3.73 (1H, d, J=13 Hz), 4.03 (1H, d, J=14 Hz), 6.66 (2H, d, J=7.6 Hz), 6.90-8.00 (10H, m), 8.57 (1H, s)

61) ^{1}H-NMR($CDCl_3$) δ ; 2.40 (3H, s), 2.90-3.20 (3H, m), 3.73 (1H, d, J=13 Hz), 4.07 (1H, d, J=13 Hz), 4.70-5.00 (1H, m), 6.60-6.80 (2H, m), 6.90-8.00 (10H, m), 8.54 (1H, s)

62) ^{1}H-NMR($CDCl_3$) δ ; 2.41 (3H, s), 2.90-3.20 (3H, m), 3.75 (1H, d, J=14 Hz), 4.08 (1H, d, J=14 Hz), 4.80-5.00 (1H, m), 6.67 (1H, d, J=7.6 Hz), 6.82 (1H, d, J=7.6 Hz), 6.90-7.90 (10H, m), 8.08 (1H, s)

63) ^{1}H-NMR($CDCl_3$) δ ; 1.23 (3H, t, J=7 Hz), 1.40-1.70 (1H, m), 1.90-2.20 (3H, m), 2.70-3.30 (3H, m), 3.40-3.60 (5H, m), 3.91 (2H, s), 5.00-5.20 (1H, m), 6.60-7.40 (11H, m), 8.12 (1H, d, J=8 Hz), 8.99 (1H, s)

64) ^{1}H-NMR($CDCl_3$) δ ; 1.35-1.70 (1H, m), 1.80-2.20 (3H, m), 2.25-2.35 (1H, m), 2.65-3.20 (3H, m), 4.01 (2H, s), 4.05-4.17 (2H, m), 4.90-5.10 (1H, m), 6.61 (1H, d, J=7.5 Hz), 6.75-7.50 (12H, m), 8.44 (1H, brs)

65) ^{1}H-NMR($CDCl_3$) δ ; 1.13 (3H, t, J=7.0 Hz), 1.30-1.65 (4H, m), 1.80-2.20 (3H, m), 2.28 (3H, s), 2.65-3.40 (5H, m), 4.90-5.10 (1H, m), 6.63 (1H, d, J=7.8 Hz), 6.75-7.00 (3H, m), 7.00-7.45 (8H, m), 8.85 (1H, brs)

66) ^{1}H-NMR($CDCl_3$) δ ; 0.88 (3H, t, J=7.4 Hz), 1.16 (3H, t, J=7.0 Hz), 1.35-2.20 (6H, m), 2.27 (3H, s), 2.60-3.20 (3H, m), 3.20-3.45 (2H, m), 3.85-4.10 (1H, m), 4.90-5.10 (1H, m), 6.63 (1H, d, J=7.4 Hz),

6.77 (2H, d, J=8.5 Hz), 6.92 (1H, t, J=8.0 Hz), 7.00-7.45 (8H, m), 8.85 (1H, brs)

67) ^{1}H-NMR($CDCl_3$) δ ; 1.17 (3H, t, J=7.0 Hz), 1.35-1.65 (4H, m), 2.60-3.45 (5H, m), 4.20 (2H, q, J=7.0 Hz), 4.90-5.10 (1H, m), 6.63 (1H, d, J=7.6 Hz), 6.80-7.45 (12H, m), 8.66 (1H, brs)

68) ^{1}H-NMR($CDCl_3$) δ ; 0.96 (6H, d, J=6.6 Hz), 1.35-1.65 (1H, m), 1.80-2.25 (4H, m), 2.65-3.15 (3H, m), 3.19 (2H, d, J=7.3 Hz), 3.99 (2H, s), 4.90-5.10 (1H, m), 6.60 (1H, d, J=7.8 Hz), 6.75-7.05 (4H, m), 7.05-7.40 (8H, m), 8.15 (1H, brs)

69) ^{1}H-NMR($CDCl_3$) δ ; 1.19 (3H, t, J=7.0 Hz), 1.35-1.65 (1H, m), 1.80-2.25 (3H, m), 2.70-3.20 (3H, m), 3.44 (2H, q, J=7.0 Hz), 3.77 (3H, s), 3.87 (2H, s), 4.90-5.10 (1H, m), 6.25-6.50 (3H, m), 6.67 (1H, d, J=7.5 Hz), 6.85-7.45 (8H, m), 8.29 (1H, brs)

70) ^{1}H-NMR($CDCl_3$) δ ; 1.05 (3H, t, J=7.1 Hz), 1.35-1.65 (1H, m), 1.85-2.25 (3H, m), 2.65-3.30 (5H, m), 3.74 (2H, s), 4.95-5.15 (1H, m), 6.63 (1H, d, J=7.5 Hz), 6.80-7.55 (11H, m), 9.51 (1H, brs)

71) ^{1}H-NMR($CDCl_3$) δ ; 1.30-1.65 (1H, m), 1.80-2.30 (3H, m), 2.65-3.15 (3H, m), 3.75 (2H, s), 3.74 (2H, s), 4.95-5.10 (1H, m), 6.45-6.70 (3H, m), 6.88 (1H, t, J=6.8 Hz), 7.00-7.45 (8H, m), 8.74 (1H, brs)

72) ^{1}H-NMR($CDCl_3$) δ ; 1.30-1.70 (1H, m), 1.75-2.25 (6H, m), 2.65-3.15 (3H, m), 3.78 (2H, d, J=5.4 Hz), 4.28

(2H, d, J=5.5 Hz), 4.53 (1H, brs), 4.90-5.10 (1H, m), 5.89 (1H, brs), 6.50-6.70 (3H, m), 6.89 (1H, t, J=7.5 Hz), 7.00-7.40 (8H, m), 8.61 (1H, brs)

73) ^{1}H-NMR($CDCl_3$) δ ; 1.35-1.65 (1H, m), 1.70-2.20 (8H, m), 2.65-3.20 (3H, m), 3.25-3.55 (4H, m), 3.88 (2H, s), 4.90-5.10 (1H, m), 5.79 (1H, brs), 6.55-7.40 (13H, m), 8.37 (1H, brs)

74) ^{1}H-NMR($CDCl_3$) δ ; 1.35-2.00 (8H, m), 2.65-3.20 (3H, m), 3.30-3.35 (2H, m), 3.60-3.85 (2H, m), 3.90 (2H, s), 4.95-5.15 (1H, m), 6.55-7.00 (5H, m), 7.00-7.40 (8H, m), 7.65-7.90 (4H, m), 8.22 (1H, brs)

75) ^{1}H-NMR($CDCl_3$) δ ; 1.16 (3H, t, J=7.0 Hz), 2.39 (3H, s), 2.80-3.20 (3H, m), 3.44 (2H, q, J=7.0 Hz), 3.65-4.20 (4H, m), 4.80-5.05 (1H, m), 6.50-7.45 (13H, m), 8.50 (1H, brs)

76) ^{1}H-NMR($CDCl_3$) δ ; 1.23 (3H, t, J=7.0 Hz), 2.41 (3H, s), 2.75-3.20 (3H, m), 3.40-3.60 (5H, m), 3.65-3.90 (1H, m), 3.92 (2H, s), 3.90-4.20 (1H, m), 4.85-5.10 (1H, m), 6.65-7.45 (11H, m), 8.13 (1H, d, J=8.4 Hz), 9.01 (1H, brs)

77) ^{1}H-NMR($CDCl_3$) δ ; 1.80-1.95 (1H, m), 2.20-2.70 (10H, m), 3.50-3.60 (1H, m), 3.63-3.80 (1H, m), 4.00-4.15 (1H, m), 6.60 (1H, d, J=7.6 Hz), 6.92 (1H, t, J=7.6 Hz), 7.02 (1H, t, J=6.3 Hz), 7.20-7.65 (9H, m), 7.87 (1H, brs)

78) ^{1}H-NMR($CDCl_3$) δ ; 1.40-1.62 (1H, m), 1.84-2.22 (3H,

m), 2.65-3.19 (3H, m), 3.97 (2H, t, J=4.9 Hz), 4.43 (2H, t, J=4.9 Hz), 4.95-5.18 (1H, m), 6.60-6.77 (1H, m), 6.85-7.02 (2H, m), 7.02-7.30 (5H, m), 7.40-7.68 (3H, m), 8.20-8.32 (1H, m), 9.62-9.81 (1H, m)

79) ^{1}H-NMR($CDCl_3$) δ ; 1.38-1.65 (1H, m), 1.84-2.21 (3H, m), 2.64-3.15 (3H, m), 3.81 (2H, t, J=5.7 Hz), 4.25 (2H, t, J=5.7 Hz), 4.90-5.13 (1H, m), 6.58-6.71 (1H, m), 6.82-7.00 (1H, m), 7.00-7.52 (10H, m), 8.11 (1H, brs)

Example 513

To a solution of 1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine (1.06 g) in dichloromethane (80 ml) is added o-methylphenyl isocyanate (0.66 g) under ice-cooling. The mixture is stirred at room temperature for 4 hours. After completion of the reaction, the solvent is concentrated under reduced pressure and the resulting residue is purified by silica gel column chromatography (eluent; n-hexane : ethyl acetate = 1 : 1), and recrystallized from ethyl acetate to give 1-[4-(2-methylanilinocarbonylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.97 g) as white powder, m.p. 182 - 182.5°C.

Using the suitable starting materials, the compounds of the above Examples 491 - 492 are obtained in the same manner as in Example 513.

Example 514

A mixture of 1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine (0.50 g), phenylsulfonyl chloride (0.29 ml), triethylamine (0.32 ml) and dichloromethane (30 ml) is stirred at room temperature overnight. The reaction mixture is washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is distilled off and the resulting residue is purified by silica gel column chromatography (eluent; chloroform), and recrystallized from methanol/diethyl ether to give 1-(4-phenylsulfonylaminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine (0.27 g) as colorless prisms, m.p. 178 - 182.5°C.

Using the suitable starting materials, the compounds of the above Examples 469 - 471, 498, 502 and 503 are obtained in the same manner as in Example 514.

Example 515

To a solution of 1-[4-(4-piperidinylcarbonylamino)-benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.70 g) in dimethylformamide (20 ml) is added 60 % sodium hydride dispersion in mineral oil (82 mg) and the mixture is stirred at room temperature for 30 minutes. Thereto is added methyl iodide (0.14 ml) and the mixture is stirred ar room temperature overnight. The solvent is distilled off and the resulting residue is extracted with chloroform, and washed succcssively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is distilled off

and the resulting residue is purified by silica gel column chromatography (eluent; chloroform : methanol = 10 : 1), and recrystallized from methanol/n-hexane to give 1-{4-[N-(1-methyl-4-piperidinylcarbonyl)-N-methylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (0.03 g) as light yellow powder, m.p. 194.5 - 197°C.

Using the suitable starting materials, the compounds of the above Examples 497 and 501 are obtained in the same manner as in Example 515.

Example 516

6-Fluoro-1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline (0.15 g) is dissolved in dichloromethane (10 ml) and thereto is added triethylamine (0.31 ml). To the mixture is added dropwise a solution of 3,5-dichlorobenzoyl chloride (0.14 g) in dichloromethane (2.0 ml) under ice-cooling, and the mixture is stirred for 30 minutes under ice-cooling, and further, at room temperature for 1 hour. To the mixture are added triethylamine (0.31 ml) and 3,5-dichlorobenzoyl chloride (0.14 ml). The mixture is stirred at room temperature for 4 hours. The reaction mixture is washed with water, and dried over magnesium sulfate. The solvent is distilled off and the resulting residue is purified by silica gel column chromatography (eluent; ethyl acetate : n-hexane = 1 : 5 → 1 : 4), and recrystallized from ethyl acetate/n-hexane to give 6-fluoro-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline

(0.12 g) and 6-fluoro-1-{4-[bis-(3,5-dichlorobenzoyl)amino]-benzoyl}-1,2,3,4-tetrahydroquinoline.

The former: White powder, m.p. 205.5 - 206.5°C

The latter: White powder, m.p. 210.5 - 212°C

Example 517

Using the suitable starting materials, the compounds of the above Examples 450 and 504 are obtained in the same manner as in Example 378.

Example 518

Using the suitable starting materials, the compounds of the above Examples 450 - 467, 495, 496, 499, 500, 511 and 512 are obtained in the same manner as in Example 380.

Example 519

Using the suitable starting materials, the compounds of the above Examples 449, 474 - 489, 493 and 494 are obtained in the same manner as in Example 394.

Example 520

Using the suitable starting materials, the compounds of the above Examples 453, 455, 457, 459, 460, 463 - 467, 495, 496 and 499 are obtained in the same manner as in Example 397.

Example 521

Using the suitable starting materials, the compound of the above Example 461 is obtained in the same manner as

in Example 396.

Example 522

Using the suitable starting materials, the compound of the above Example 456 is obtained in the same manner as in Example 398.

Example 523

Using the suitable starting materials, the compound of the above Example 459 is obtained in the same manner as in Example 399.

Example 524

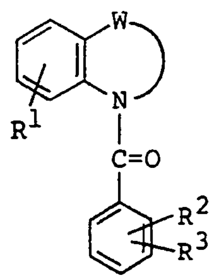
Using the suitable starting materials, the compounds of the above Examples 495 and 496 are obtained in the same manner as in Examples 400 and 401.

Example 525

Using the suitable starting materials, the compound of the above Example 458 is obtained in the same manner as in Example 402.

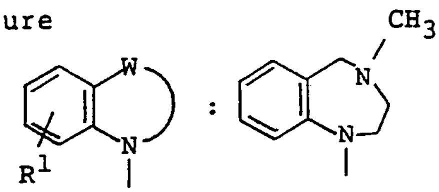
Using the suitable starting materials, the compounds of the following Table 3 are obtained in the same manner as in Examples 1 and 382.

Table 3

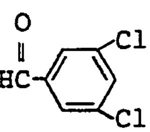


Example 527

Structure



R^2: 2-Cl

R^3: 4-NHC(=O)-


Crystalline form: White powder

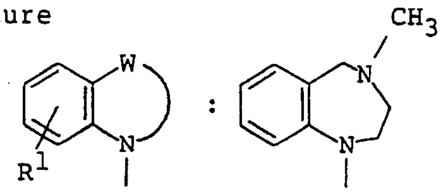
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 225 - 226°C

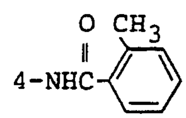
Form: Free

Example 528

Structure



R^2: 2-Cl

R^3: 

Crystalline form: White powder

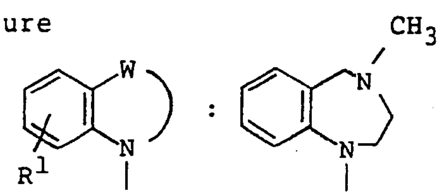
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 142.5 - 145°C

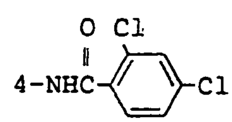
Form: Free

Example 529

Structure



R^2: 2-Cl

R^3: 

Crystalline form: White powder

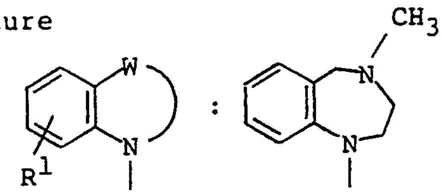
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 213 - 215°C

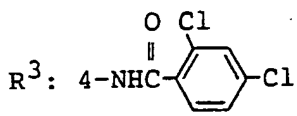
Form: Free

Example 530

Structure



R^2: 3-CH_3



Crystalline form: White powder

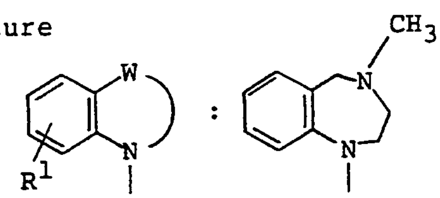
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 167 - 167.5°C

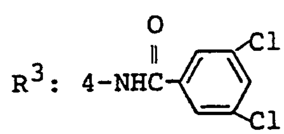
Form: Free

Example 531

Structure



R^2: 3-CH_3



Crystalline form: Colorless scales

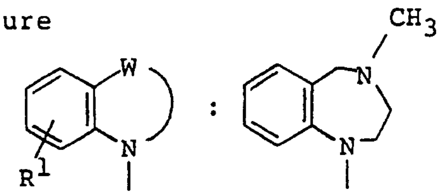
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 217 - 221°C

Form: Free

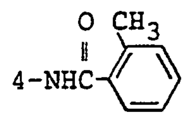
Example 532

Structure



R^2: 3-CH_3

R^3:



Crystalline form: White powder

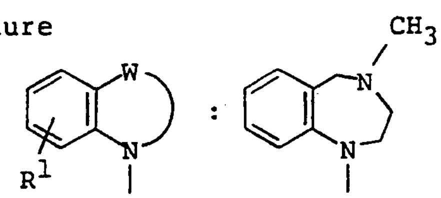
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 182 - 184°C

Form: Free

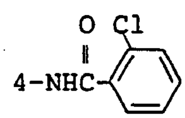
Example 533

Structure



R^2: 3-CH_3

R^3:



Crystalline form: White powder

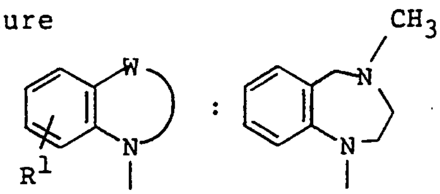
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 209 - 210°C

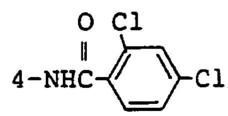
Form: Free

Example 534

Structure



R^2: 3-OCH_3

R^3: 

Crystalline form: White powder

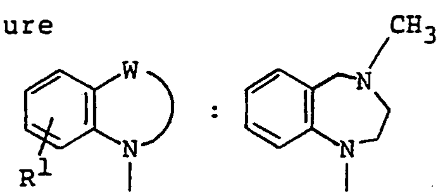
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 148 - 149°C

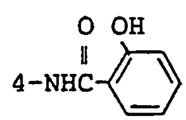
Form: Free

Example 535

Structure



R^2: H

R^3: 

Crystalline form: White powder

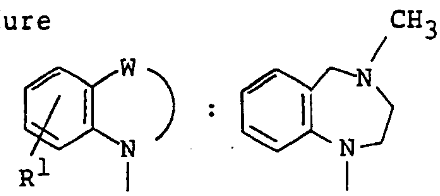
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 202 - 203°C

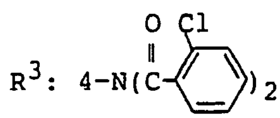
Form: Free

Example 536

Structure



R^2: 3-CH_3



Crystalline form: White powder

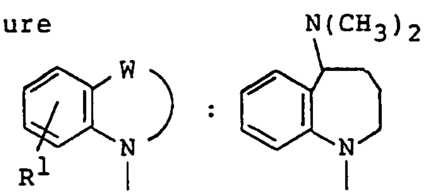
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 218 - 219°C

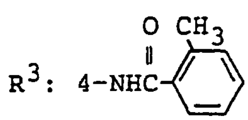
Form: Free

Example 537

Structure



R^2: 2-Cl



Crystalline form: White powder

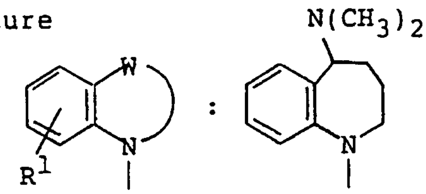
Recrystallization solvent: Methanol/n-hexane

Melting Point: 159 - 160°C

Form: Free

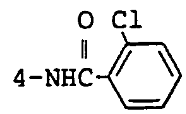
Example 538

Structure



R^2: 2-Cl

R^3:



Crystalline form: White powder

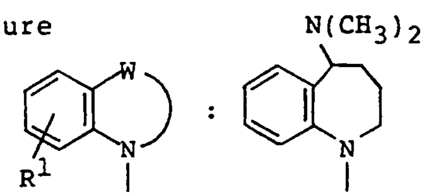
Recrystallization solvent: Methanol/n-hexane

Melting Point: 201 - 202°C

Form: Free

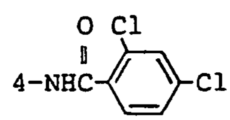
Example 539

Structure



R^2: 2-Cl

R^3:



Crystalline form: White powder

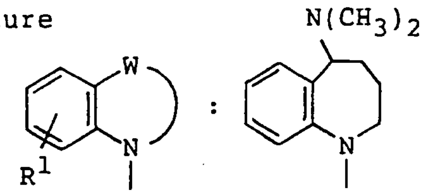
Recrystallization solvent: Methanol/n-hexane

Melting Point: 205 - 207°C

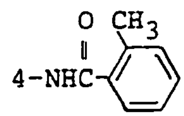
Form: Free

Example 540

Structure



R^2: 3-OH

R^3: 

Crystalline form: White powder

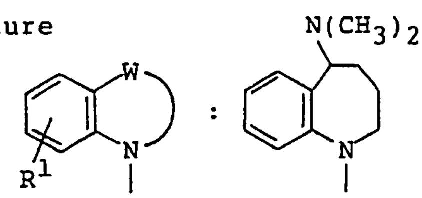
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 201.5 - 202.5°C

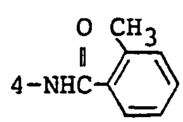
Form: Free

Example 541

Structure



R^2: 2-OCH_3

R^3: 

Crystalline form: White powder

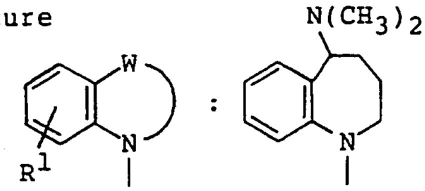
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 226 - 228°C

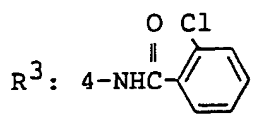
Form: Free

Example 542

Structure



R^2: 2-OCH_3



Crystalline form: White powder

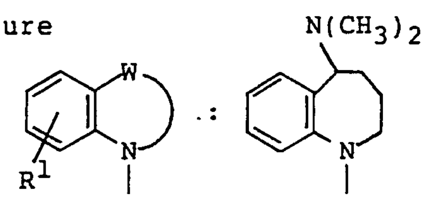
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 218 - 221°C

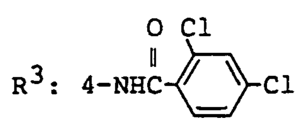
Form: Free

Example 543

Structure



R^2: 2-OCH_3



Crystalline form: White powder

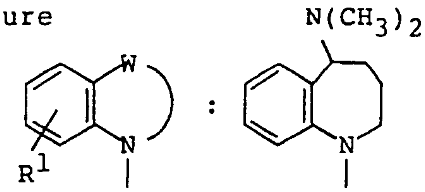
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 156 - 157°C

Form: Free

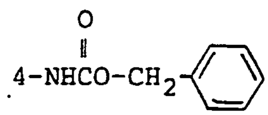
Example 544

Structure



R^2: 2-OCH_3

R^3:



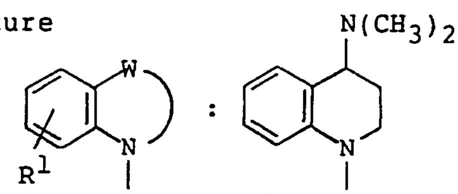
Crystalline form: White powder

NMR analysis: 80)

Form: Free

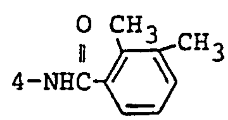
Example 545

Structure



R^2: 3-OCH_3

R^3:



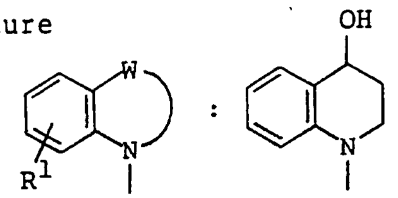
Crystalline form: Colorless amorphous

NMR analysis: 81)

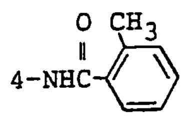
Form: Free

Example 546

Structure



R^2: H

R^3: 

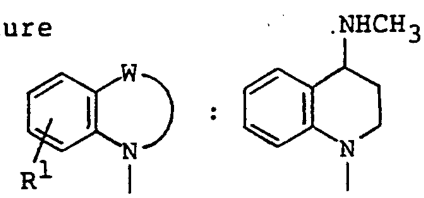
Crystalline form: Colorless amorphous

NMR analysis: 82)

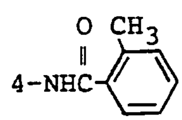
Form: Free

Example 547

Structure



R^2: H

R^3: 

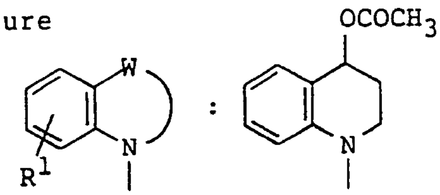
Crystalline form: Light yellow amorphous

NMR analysis: 83)

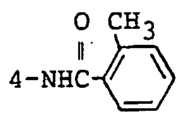
Form: Free

Example 548

Structure



R^2: H

R^3: 

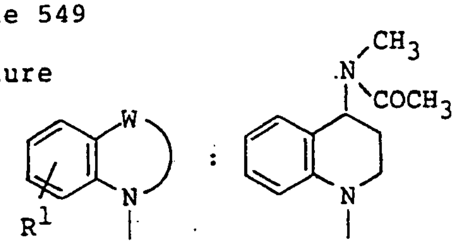
Crystalline form: Colorless amorphous

NMR analysis: 84)

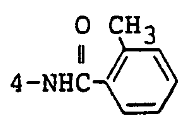
Form: Free

Example 549

Structure



R^2: H

R^3: 

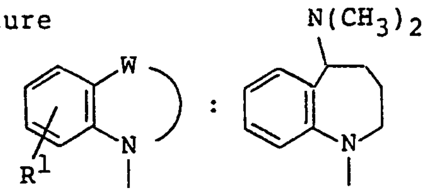
Crystalline form: Colorless amorphous

NMR analysis: 85)

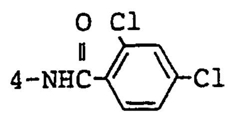
Form: Free

Example 550

Structure



R^2: 3-OCH_2CH_3

R^3: 

Crystalline form: White powder

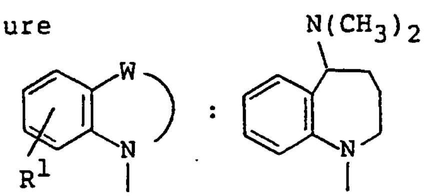
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 135 - 136°C

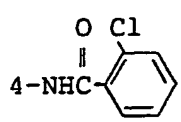
Form: Free

Example 551

Structure



R^2: 3-OCH_2CH_3

R^3: 

Crystalline form: Colorless prisms

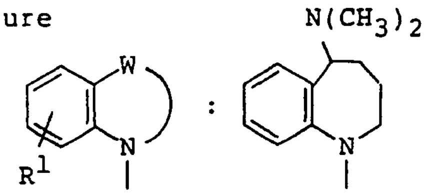
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 122 - 123°C

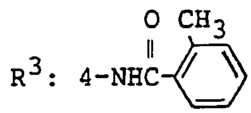
Form: Free

Example 552

Structure



R^2: 3-OCH_2CH_3



Crystalline form: Colorless prisms

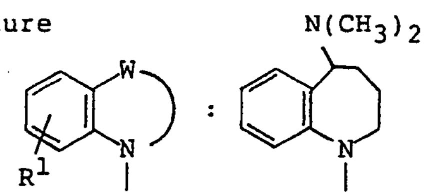
Recrystallization solvent: n-Hexane/ethyl acetate

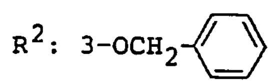
Melting Point: 118 - 119°C

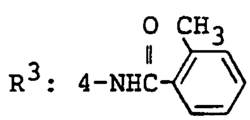
Form: Free

Example 553

Structure







Crystalline form: Colorless prisms

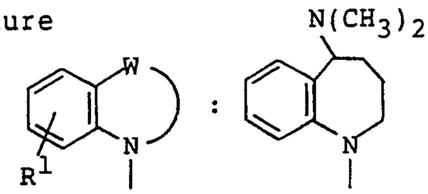
Recrystallization solvent: n-Hexane/ethyl acetate

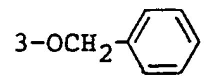
Melting Point: 145 - 147°C

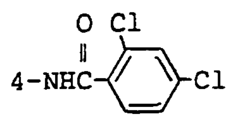
Form: Free

Example 554

Structure



R^2: 

R^3: 

Crystalline form: Light yellow needles

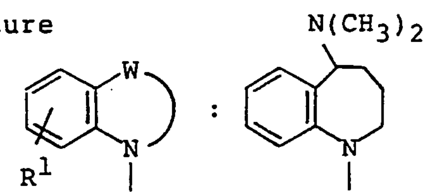
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 169.5 - 170.5°C

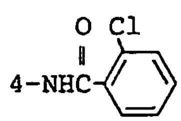
Form: Free

Example 555

Structure



R^2: 3-OH

R^3: 

Crystalline form: Colorless prisms

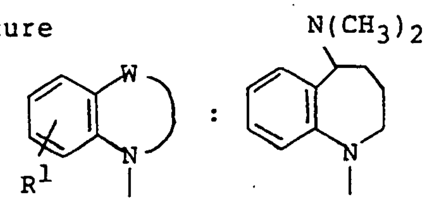
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 194 - 195°C

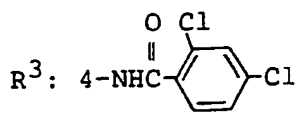
Form: Free

Example 556

Structure



R^2: 3-OH



Crystalline form: Colorless needles

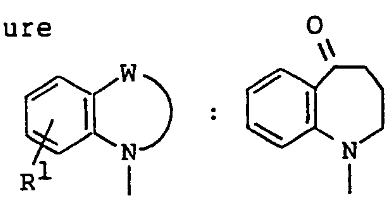
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 202 - 204°C

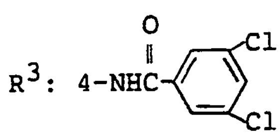
Form: Free

Example 557

Structure



R^2: H



Crystalline form: Colorless prisms

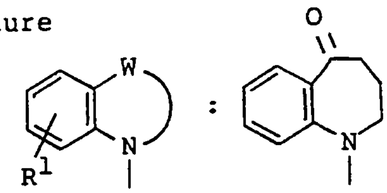
Recrystallization solvent: Ethanol

Melting Point: 242 - 243°C

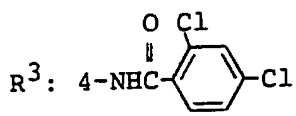
Form: Free

Example 558

Structure



R^2: H



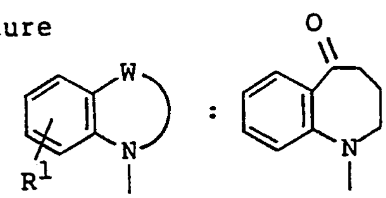
Crystalline form: Light yellow powder

NMR analysis: 86)

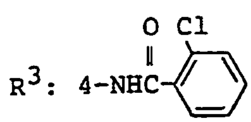
Form: Free

Example 559

Structure



R^2: H



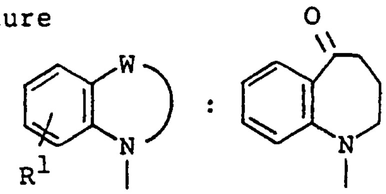
Crystalline form: Light yellow powder

NMR analysis: 87)

Form: Free

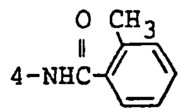
Example 560

Structure



R^2: H

R^3:



Crystalline form: Colorless needles

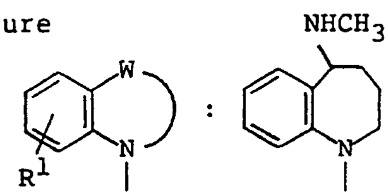
Recrystallization solvent: Ethanol

Melting Point: 237 - 238°C

Form: Free

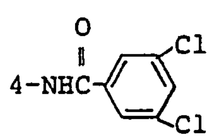
Example 561

Structure



R^2: H

R^3:



Crystalline form: Colorless prisms

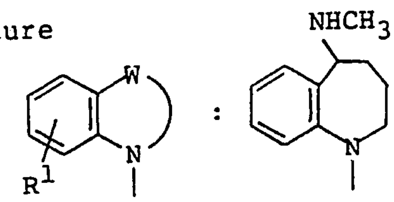
Recrystallization solvent: Dioxane

Melting Point: 258 - 259°C

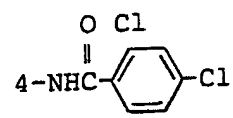
Form: Free

Example 562

Structure



R^2: H

R^3: 

Crystalline form: Colorless prisms

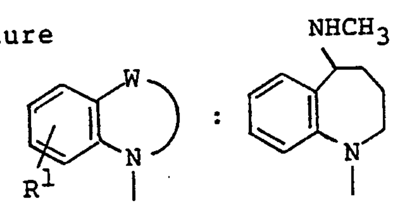
Recrystallization solvent: Ethanol

Melting Point: 182.5 - 183.5°C

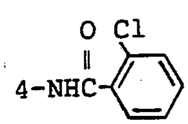
Form: Free

Example 563

Structure



R^2: H

R^3: 

Crystalline form: Colorless prisms

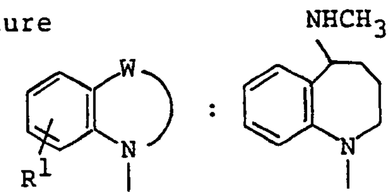
Recrystallization solvent: Ethanol

Melting Point: 209 - 211°C

Form: Free

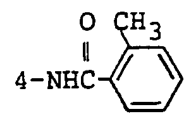
Example 564

Structure



R^2: H

R^3:



Crystalline form: Colorless prisms

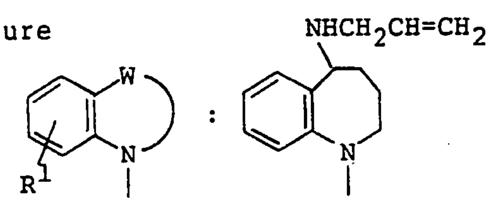
Recrystallization solvent: Dioxane

Melting Point: 210 - 211°C

Form: Free

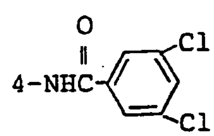
Example 565

Structure



R^2: H

R^3:



Crystalline form: Colorless needles

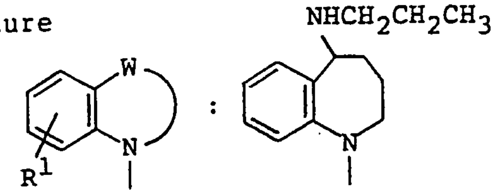
Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 176 - 178°C

Form: Free

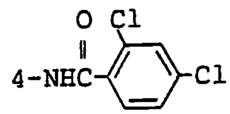
Example 566

Structure



R^2: H

R^3:



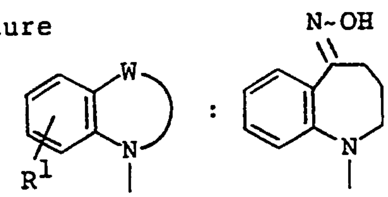
Crystalline form: Light yellow amorphous

NMR analysis: 88)

Form: Free

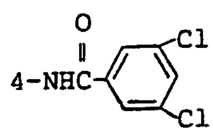
Example 567

Structure



R^2: H

R^3:



Crystalline form: White powder

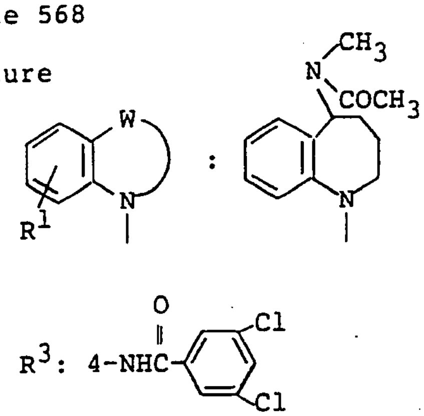
Recrystallization solvent: Dioxane/water

Melting Point: 272 - 273°C

Form: Free

Example 568

Structure



R^2: H

Crystalline form: Colorless prisms

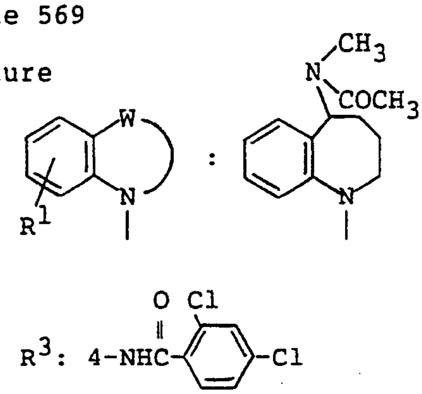
Recrystallization solvent: Dioxane

Melting Point: 253 - 254°C

Form: Free

Example 569

Structure



R^2: H

Crystalline form: Colorless prisms

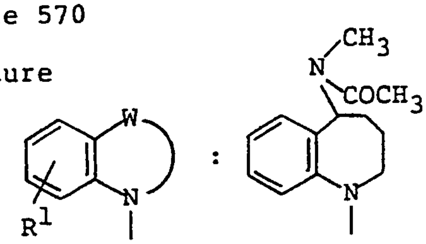
Recrystallization solvent: Ethanol

Melting Point: 248.5 - 249.5°C

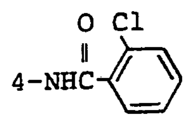
Form: Free

Example 570

Structure



R^2: H

R^3: 

Crystalline form: Colorless needles

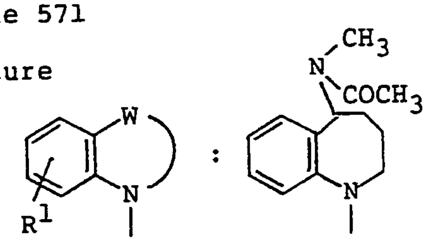
Recrystallization solvent: Ethanol

Melting Point: 266.5 - 267.5°C

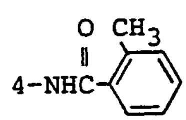
Form: Free

Example 571

Structure



R^2: H

R^3: 

Crystalline form: Colorless needles

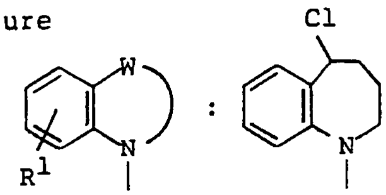
Recrystallization solvent: Ethanol

Melting Point: 252 - 253°C

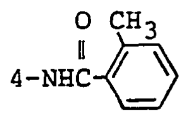
Form: Free

Example 572

Structure



R^2: H

R^3: 

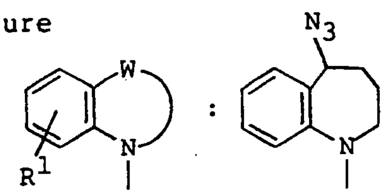
Crystalline form: Light yellow powder

NMR analysis: 89)

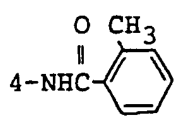
Form: Free

Example 573

Structure



R^2: H

R^3: 

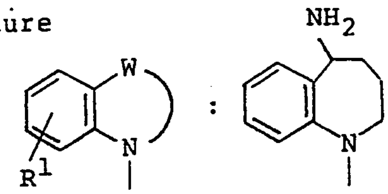
Crystalline form: Light brown powder

NMR analysis: 90)

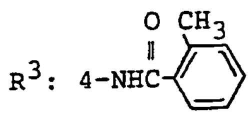
Form: Free

Example 574

Structure



R^2: H



Crystalline form: White powder

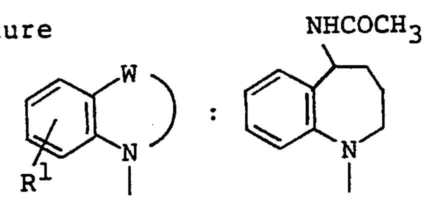
Recrystallization solvent: Diethyl ether

Melting Point: 198.5 - 199.5°C

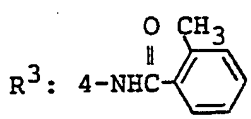
Form: Free

Example 575

Structure



R^2: H



Crystalline form: Colorless needles

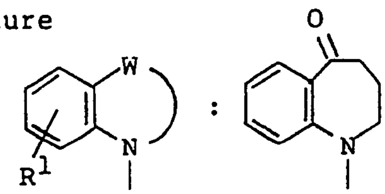
Recrystallization solvent: Ethanol

Melting Point: 297 - 299°C

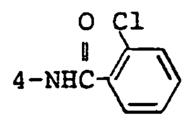
Form: Free

Example 576

Structure



R^2: 2-Cl

R^3:


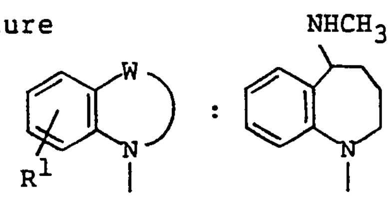
Crystalline form: Colorless amorphous

NMR analysis: 91)

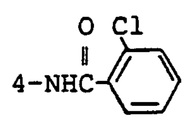
Form: Free

Example 577

Structure



R^2: 2-Cl

R^3:


Crystalline form: White powder

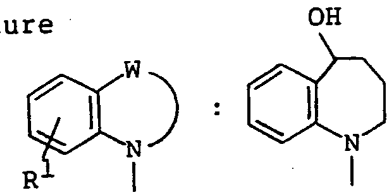
Recrystallization solvent: Ethanol/petroleum ether

Melting Point: 202 - 203°C

Form: Free

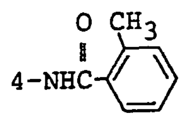
Example 578

Structure



R^2: H

R^3:



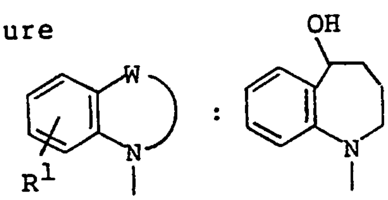
Crystalline form: Colorless amorphous

NMR analysis: 92)

Form: Free

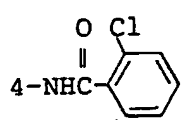
Example 579

Structure



R^2: H

R^3:



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 232 - 233°C

Form: Free